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WOMEN VIETNAM VETERANS HEALTH STUDY
PROTOCOL DEVELOPMENT

CONTRACT NO. V101(93)P-1138

STUDY DESIGN AND PROTOCOL
APPENDICES
DELIVERABLE D

SUBMITTED BY NEW ENGLAND RESEARCH INSTITUTE

PRINCIPAL INVESTIGATOR
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STUDY DESIGN PROTOCOL

APPENDICES

DELIVERABLE D

1. INFORMED CONSENT AND RELEASE FORMS
2. CONGENITAL ABNORMALITY CLASSIFICATION AND PEDIATRIC EXAMINATION
3. MYOCARDIAL INFARCTION, SUDDEN DEATH AND STROKE CLASSIFICATION
4. NEUROBEHAVIORAL TESTING PROTOCOL
5. SOFT TISSUE SARCOMA CLASSIFICATION
6. PROTOCOL FOR 2, 3, 7, 8 - TCDD BODY BURDEN DETERMINATION

I N F O R M E D C O N S E N T
A N D R E L E A S E F O R M S

date

Name
Street Address
City, State, Zip

Dear _____:

As part of the "Women Veterans Health Study" sponsored by the Veterans Administration, we are interested in obtaining complete medical records on your hospitalizations which include some more technical information that is needed for the study.

As we told you over the telephone, in order to do that we need to obtain a signed authorization form from you first. Could you please help us by signing the enclosed authorization form and returning it to us in the enclosed envelope as soon as possible. You may be assured that the information will be kept confidential and will be used only in completing the review of your record.

We will be most grateful for your cooperation.

Sincerely yours,

Contractor

Written Release Format and Record RequestAUTHORIZATION FOR DISCLOSURE OF MEDICAL INFORMATION

Name: _____ Hospital Number: _____
Address: _____ Date of Birth: _____

I hereby authorize the _____ Hospital/Clinic to
release information from my medical records to:

CONTRACTOR
ADDRESS

This authorization covers all medical and/or psychiatric
treatment, history of illness or related information. This
authorization shall remain in effect as long as necessary
(up to one year) to respond to the attached request. I also
understand that I may revoke this authorization at any time.

This authorization expires one year from date signed.

Signature of Patient: _____ Date: _____

Authorization received by: _____ Office: _____

WOMEN VETERANS HEALTH STUDY

7/1/87

INFORMED CONSENT (PARTICIPANTS)

As a participant in the "Women Veterans Health Study" I understand that I am eligible to participate in a follow-up study, on a subsample of individuals funded by the Veterans Administration. This follow-up is being conducted by (Contractor) in collaboration with the Red Cross. It includes collecting information on neuropsychological behavior, and physiological measurements.

I understand that as a participant in this study, I will be asked to provide answers to some health-related questions, and participate in neurological testing which will be completed in a home visit, at my convenience, in about 3 hours.

I understand that a visit to the nearest Red Cross Center will be scheduled for a blood sample to measure TCDD (dioxin) levels. Risks from the measurement made at the Red Cross Center includes slight discomfort at the insertion of the needle for the blood sample, and a small chance of bruising and infection. This procedure is similar to a donation of blood.

The results of my measurements will be provided to me in a summary report about 3 months after the visit. At my request, a copy of this report will be sent to my physician. I also understand that these tests do not replace a physical examination by a physician, and in no way do they imply any form of medical treatment or diagnosis.

I understand that all information I give is confidential and will be used for statistical purposes only. Each of these tests and procedures and their risks and discomforts have been explained to me and all of my questions about the study have been answered to my fullest satisfaction.

(Respondent) Signature

Examining Physician Signature

Date

date

Name
Street Address
City, State, Zip

Dear _____:

As part of the "Women Veterans Health Study" sponsored by the Veterans Administration, we are interested in obtaining complete medical records on your child's hospitalizations which include some more technical information that is needed for the study.

As we told you over the telephone, in order to do that we need to obtain a signed authorization form from you first. Could you please help us by signing the enclosed authorization form and returning it to us in the enclosed envelope as soon as possible. You may be assured that the information will be kept confidential and will be used only in completing the review of your child's record.

We will be most grateful for your cooperation.

Sincerely yours,

Contractor

7/1/87

INFORMED CONSENT (CHILDREN)

As a participant in the "Women Veterans Health Study" I understand that my child is eligible to participate in a follow-up study, on a subsample of offspring funded by the Veterans Administration. This follow-up is being conducted by (Contractor) in collaboration with the Red Cross. It includes examination of my child by a physician specialist.

I understand that as a participant in this study, my child will be given an examination. This will be completed in a home visit, at my and my child's convenience, in no more than 2 hours.

The results of my child's exam will be provided to me in a summary report about 3 months after the visit. At my request, a copy of this report will be sent to my child's physician. I also understand that these tests do not replace a physical examination by a physician, and in no way do they imply any form of medical treatment or diagnosis.

I understand that all information gathered is confidential and will be used for statistical purposes only. Each of these tests and procedures and their risks and discomforts have been explained to me and all of my questions about the study have been answered to my fullest satisfaction.

I give my consent to have my child, (NAME) examined by Dr. (NAME).

 Parent (Guardian) Signature

 Date

 Examining Physician Signature

 Date

Written Release Format and Record Request For Child's
Medical Records

AUTHORIZATION FOR DISCLOSURE OF MEDICAL INFORMATION

Name: _____ Hospital Number: _____

Address: _____ Date of Birth: _____

I hereby authorize the _____ Hospital/Clinic to
release information from my child's medical records to:

CONTRACTOR
ADDRESS

This authorization covers all medical and/or psychiatric
treatment, history of illness or related information. This
authorization shall remain in effect as long as necessary
(up to one year) to respond to the attached request. I also
understand that I may revoke this authorization at any time.

This authorization expires one year from date signed.

Signature of Parent: _____ Date: _____

Authorization received by: _____ Office: _____

CONGENITAL ABNORMALITY

CLASSIFICATION AND

PEDIATRIC EXAMINATION

VERIFICATION OF CONGENITAL ABNORMALITY

Currently the Ranch Hand II Study is relying on records and recoding of these records using modified ICD-9 CM classifications to verify congenital abnormalities detected up to the age of 18 years. Very few hospital records, from up to 18 years ago are unavailable. The following records are solicited:

- Birth Certificate;
- Hospital Delivery Record; and
- Records for any hospitalizations related to diagnoses of an anomaly.

The modified ICD-9 CM classification which follows and the protocol for record abstraction used on Ranch Hand II are proposed for use in this study.

BIRTH DEFECTS BRANCH SIX DIGIT CODE
For Reportable Congenital Anomalies

Based on B.P.A. Classification of Diseases
(1979) and W.H.O. I.C.D.9 CM (1977)

Code modifications developed by Birth Defects & Genetic Diseases Branch
Center for Environmental Health
Centers for Disease Control
Atlanta, Georgia 30333

Doc. No. 6digit
Version 05/87

INDEX TO 6-DIGIT CODE

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Other congenital anomalies of the digestive system	751	20-22
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.....other anomalies, upper limbs		33
.....other anomalies, lower limbs		34
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.....of skull and face bones (craniosynostosis)		36
.....of the spine and ribs		37
.....spina bifida occulta		37
.....chondrodystrophy		38
.....osteodystrophies		38
.....of the diaphragm		39
.....of the abdominal wall		39
.....other specified/unspec.		39
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Explanation to Six Digit Code

6th Digit Code - Master

- .000 Blank
- .001 Left Only
- .002 Right Only
- .003 Unilateral Unspecified
- .004 Bilateral
- .005 -
- .006 -
- .007 -
- .008 Possible or Probable
- .009 NOS

The above sixth digit added by the record abstractor to the B.P.A. Classification of Diseases code is used for the following reasons:

- .001 specify laterality if the location of the defect is known
- .002
- .003 specify if the defect is unilateral, when the specific location is unknown
- .004 specify that the defect is bilateral (ie. on both sides)
- .005 use in certain circumstances to more specifically
- .006 define a particular defect. For example, these codes may be
- .007 created to specify the location of a myelomeningocele in spina bifida as cervico-thoracic, thoraco-lumbar, or lumbo-sacral (see 741.085, etc.)
- .008 use this code specification rarely; it is available for defects which are specified as probable or possible from the hospital record.
eg. "probable PDA" = 747.008, "probable VSD" = 745.498, or a case of Down syndrome without cytogenetic verification. Medical records of cases with this defect code should be reviewed periodically in order to update the defect list with the most definitive diagnosis
- .009 specify that the defect is "not otherwise specified" in any other part of the six-digit code.

Notes:

An asterisk (*) beside a disease code indicates that the code was created by CDC.

A pound (#) beside a disease code indicates that the condition or defect is listed on the CDC Exclusion list. Use of the code should be according to the exclusion list criteria.

CONGENITAL ANOMALIES

Anencephalus and Similar Anomalies

- 740.0 Anencephalus
 - 740.000 Absence of brain
 - 740.010 Acrania
 - 740.020 Anencephaly
 - 740.030 Hemianencephaly, hemiccephaly
 - 740.080 Other
- 740.1 740.100 Craniorachischisis
- 740.2 Iniencephaly
 - 740.200 Closed iniencephaly
 - 740.210 Open iniencephaly
 - 740.290 Unspecified iniencephaly

741

Spina Bifida

Includes:

Spina bifida aperta (open lesions)

myelocele

rachischisis

Spina bifida cystica (closed lesions)

meningocele

meningomyelocele

myelomeningocele

Excludes:

Spina bifida occulta (see 756.100)

craniorachischisis (see 740.100)

741.0

Spina Bifida with Hydrocephalus

- 741.000 Spina bifida aperta, any site, with hydrocephalus
- 741.010 Spina bifida cystica, any site, with hydrocephalus and Arnold Chiari malformation "Arnold Chiari malformation NOS"
- 741.020 Spina bifida cystica, any site, with stenosed aqueduct of Sylvius
- 741.030 Spina bifida cystica, cervical, with unspecified hydrocephalus
Spina bifida cystica, cervical, with hydrocephalus but without mention of Arnold Chiari malformation or aqueduct stenosis
- 741.040 Spina bifida cystica, thoracic, with unspecified hydrocephalus, no mention of Arn.-Chiari
- 741.050 Spina bifida cystica, lumbar, with unspecified hydrocephalus, no mention of Arn.-Chiari
- 741.060 Spina bifida cystica, sacral, with unspecified hydrocephalus, no mention of Arn.-Chiari
- 741.070 Spina bifida of any site with hydrocephalus of late onset
- 741.080 Other Spina bifida, meningocele of specified site with hydrocephalus
- 741.085 Spina bifida, meningocele, cervico thoracic, with hydrocephalus
- 741.086 Spina bifida, meningocele thoraco-lumbar, with hydrocephalus
- 741.087 Spina bifida, meningocele, lumbo-sacral with hydrocephalus
- 741.090 Spina bifida of any unspecified type with hydrocephalus

- 741.9 Spina bifida without mention of hydrocephalus
- 741.900 Spina bifida (aperta), without hydrocephalus
- 741.910 Spina bifida (cystica), cervical, without hydrocephalus
- 741.920 Spina bifida (cystica), thoracic, without hydrocephalus
- 741.930 Spina bifida (cystica), lumbar, without hydrocephalus
- 741.940 Spina bifida (cystica), sacral, without hydrocephalus
- 741.980 Spina bifida, oth specified site, without hydrocephalus
- Includes:
- cervicothoracic, thoracolumbar, lumbro-sacral
- 741.985 Lipomyelomeningocele
- 741.990 Spina bifida, site unspecified, without hydrocephalus (myelocoele, myelomeningocele, meningomyelocoele)
- 742 Other Congenital Anomalies of Nervous System
- 742.0 Encephalocele
- 742.000 Occipital encephalocele
- 742.080 Other encephalocele of specified site (includes Midline defects)
- 742.085 Frontal encephalocele
- 742.086 Parietal encephalocele
- 742.090 Unspecified encephalocele
- 742.1 742.100 Microcephalus
- 742.2 Reduction deformities of brain
- 742.200 Anomalies of cerebrum
- 742.210 Anomalies of corpus callosum
- 742.220 Anomalies of hypothalamus
- 742.230 Anomalies of cerebellum
- 742.240 Agyria and lissencephaly
- 742.250 Microgyria, polymicrogyria
- 742.260 Holoprosencephaly
- 742.270 Arrhinencephaly
- 742.280 Other specified reduction defect brain
- 742.290 Unspecified reduction defect of brain
- 742.3 Congenital hydrocephalus
- Excludes: hydrocephalus with any condition in 741.9 (741.0)
- 742.300 Anomalies of aqueduct of Sylvius
- 742.310 Atresia of foramina of Magendie and Luschka
Dandy-Walker syndrome
- 742.320 Hydranencephaly
- 742.380 Other specified hydrocephaly
- Includes: "communicating hydrocephaly"
- # 742.385 Hydrocephalus secondary to intraventricular hemorrhage (IVH) or CNS bleed
- 742.390 Unspecified hydrocephaly, NOS

- 742.4 Other specified anomalies of brain
 - 742.400 Enlarged brain and/or head
 - Megalencephaly
 - Macrocephaly
 - 742.410 Porencephaly
 - Includes: porencephalic cysts
 - 742.420 Multiple cerebral cysts
 - 742.480 Other specified anomalies of brain
 - Includes: cortical atrophy
 - cranial nerve defects
 - 742.485 Ventricular cysts:
 - Excludes: arachnoid cysts (348.000)
 - 742.486 "small brain"

- 742.5 Other specified anomalies of spinal cord
 - Excludes: syringomyelia (336.000)
 - 742.500 Amyelia
 - 742.510 Hypoplasia and dysplasia of spinal cord
 - atelomyelia
 - myelodysplasia
 - 742.520 Diastematomyelia
 - 742.530 Other cauda equina anomalies
 - 742.540 Hydromyelia
 - Hydrorhachis
 - 742.580 Other specified anomalies of spinal cord and membranes

- 742.8 Other specified anomalies of nervous system
 - Excludes: congenital oculofacial paralysis
 - "moebius syndrome" (352.600)
 - 742.800 Jaw-winking syndrome
 - Marcus Gunn syndrome
 - 742.810 Familial dysautonomia
 - Riley-Day syndrome
 - 742.880 Other specified anomalies of nervous system

- 742.9 Unspecified anomalies of brain, spinal cord and nervous systems
 - 742.900 Brain, unspecified anomalies
 - 742.910 Spinal cord, unspecified anomalies
 - 742.990 Nervous system, unspecified anomalies

743 Congenital Anomalies of Eye

743.000 Anophthalmos
 agenesis of eye cryptophthalmos

743.100 Microphthalmos, small eyes
 aplasia of eye hypoplasia of eye
 dysplasia of eye rudimentary eye

743.2 Buphthalmos

743.200 Buphthalmos
 congenital glaucoma
 hydrophthalmos

743.210 Enlarged eye NOS

743.220 Enlarged cornea
 keratoglobus
 congenital megalocornea

743.3 Congenital cataract and lens anomalies

743.300 Absence of lens
 congenital aphakia

743.310 Spherical lens
 Spherophakia

743.320 Cataract, NOS

743.325 Cataract anterior polar

743.326 Cataract, other specified

743.330 Displaced lens

743.340 Coloboma of lens

743.380 Other specified lens anomalies

743.390 Unspecified lens anomalies

743.4 Coloboma and other anomalies of anterior segments

743.400 Corneal opacity

743.410 Other corneal anomalies
 Excludes: megalocornea (743.220)

743.420 Absence of iris
 aniridia

743.430 Coloboma of iris

743.440 Other anomalies of iris
 polycoria
 ectopic pupil
 Peter's anomaly

743.450 Blue Sclera

743.480 Other spec colobomas and anom. of ant. segments
 Rieger's anomaly
 coloboma of optic disc

743.490 Unspecified colobomas and anomalies of anterior eye
 segments

- 743.5 Congenital anomalies of posterior segment
- 743.500 Specified anomalies of vitreous humour
- 743.510 Specified anomalies of retina
 congenital retinal aneurysm
- 743.520 Specified anomalies of optic disc
 hypoplastic optic nerve
- 743.530 Specified anomalies of choroid
- 743.535 Coloboma of choroid
- 743.580 Other spec anomalies of posterior segment of eye
- 743.590 Unspecified anomalies of posterior segment of eye
- 743.6 Congenital anomalies of eyelids, lacrimal system
 and orbit
- 743.600 Blepharoptosis
 congenital ptosis
- 743.610 Ectropion
- 743.620 Entropion
- 743.630 Other anomalies of eyelids
 fused eyelids absence of eyelashes
 long eyelashes weakness of eyelid
- 743.635 Blepharophimosis
 small or narrow palpebral fissures
- 743.636 Coloboma of the eyelids
- 743.640 Absence or agenesis of lacrimal apparatus
 absence of punctum lacrimale
- * 743.650 Stenosis or stricture of lacrimal duct
- 743.660 Other anomalies of lacrimal apparatus, e.g. cyst
- 743.670 Anomalies of orbit
- 743.8
- * 743.800 Other specified anomalies of eye
 Includes:
 exophthalmos epicanthal folds
 antimongoloid slant upward eyeslant
 Excludes:
 congenital nystagmus (379.500)
 retinitis pigmentosa (362.700)
 ocular albinism (270.200)
 wide spaced eyes, hypertelorism (756.020)
- * 743.810 Epibulbar dermoid cyst
- 743.9 743.900 Unspecified anomalies of eye
 Congenital: of eye (any part)
 Anomaly NOS
 Deformity NOS

744 Congenital Anomalies of Ear, Face and Neck

744.0 Anomalies of ear causing impairment of hearing

744.000 Absence or stricture of auditory canal

744.010 Absence of auricle (Pinna)
absence of ear NOS

744.020 Anomaly of middle ear
fusion of ossicles

744.030 Anomaly of inner ear
Includes: congenital anomaly of:
membranous labyrinth
organ of Corti

744.090 Unspec anomalies of ear with hearing impairment
Includes: congenital deafness, NOS

744.1 Accessory auricle

744.100 Accessory auricle
Polyotia

744.110 Preauricular appendage, tag or lobule
(in front of ear canal)

744.120 Other appendage, tag or lobule include papillomas,
ear tags

744.2 Other specified anomalies of ear

744.200 Macrotia (enlarged pinna)

744.210 Microtia, (hypoplastic pinna and absence or
stricture of external auditory meatus)

744.220 Bat ear

744.230 Other misshapen ear
pointed ear elfin pixie-like
lop ear cauliflower ear
cleft in ear malformed ear
absent or decreased cartilage

744.240 Misplaced ears

744.245 Low Set Ears

744.246 Posteriorly rotated ears

744.250 Absence or anomaly of eustachian tube

744.280 Other spec anomalies of ear (see also 744.230)
Darwin's tubercle

744.3	744.300	Unspecified anomalies of ear Congenital: ear (any part) anomaly, deformity NOS
744.4		Branchial cleft, cyst or fistula; preauricular sinus
	744.400	Branchial cleft, sinus, fistula cyst or pit
	744.410	Preauricular sinus, cyst or pit
	744.480	Other branchial cleft anomalies, include dermal sinus of head
	# 744.500	Webbing of neck Pterygium colli
744.8		Other specified anomalies of face and neck
	744.800	Macrostomia (large mouth)
	744.810	Microstomia (small mouth)
	744.820	Macrocheilia (large lips)
	744.830	Microcheilia (small lips)
	744.880	Other specified anomalies of face/neck
744.9		Unspecified anomalies of face and neck
	744.900	Congenital anomaly of neck NOS Includes: short neck
	# 744.910	Congenital anomaly of face NOS Abnormal facies

- 745 Bulbus Cordis Anomalies and Anomalies of Cardiac Septal Closure
- 745.0 Common truncus (see 747.200 for pseudotruncus)
 - 745.000 Persistent truncus arteriosus
 - absent septum between aorta and pulmonary artery
 - 745.010 Aortic septal defect
 - Includes: aortopulmonary window
 - Excludes:
 - atrial septal defect (use 745.590)
- 745.1 Transposition of great vessels
 - 745.100 Transposition of great vessels, complete (no VSD)
 - 745.110 Transposition of great vessels, incomplete (w/ VSD)
 - Taussig-Bing syndrome
 - 745.120 Corrected transposition of great vessels,
 - L-transposition, ventri in version
 - Excludes:
 - dextrocardia (use 746.800)
 - 745.180 Other spec transposition of great vessels
 - Includes:
 - double outlet right ventricle
 - 745.190 Unspecified transposition of great vessels
- 745.2 Tetralogy of Fallot
 - 745.200 Fallot's tetralogy
 - 745.210 Fallot's pentalogy
 - Fallot's tetralogy plus atrial septal defect (ASD)
- 745.3 745.300 Single ventricle
 - Common ventricle
 - Cor triloculare biatriatum

745.4 Ventricular septal defect

745.400 Roger's disease

745.410 Eisenmenger's syndrome

745.420 Gerbode defect

745.480 Other specified ventricular septal defect

745.490 VSD (ventricular septal defect),NOS
 Excludes: common atrioventricular canal
 type (use 745.620)

745.498 Probable VSD

745.5 Ostium secundum type atrial septal defect

745.500 Nonclosure of foramen ovale NOS
 Patent foramen ovale

745.510 Ostium (septum) secundum defect

745.520 Lutembacher's syndrome

745.580 Other specified atrial septal defect

745.590 ASD (atrial septal defect) NOS
 Auricular septal defect NOS
 Partial foramen ovale

745.6 Endocardial cushion defects

745.600 Ostium primum defects

745.610 Single common atrium, cor triloculare biventriculare

745.620 Common atrioventricular canal
 with ventricular septal defect (VSD)

745.630 Common atrioventricular canal

745.680 Other specified cushion defect

745.690 Endocardial cushion defect NOS

745.7 745.700 Cor biloculare

745.8 745.800 Other specified defects of septal closure

745.9 745.900 Unspecified defect of septal closure

- 746 Other Congenital Anomalies of Heart
- 746.0 Anomalies of pulmonary valve
 - 746.000 Atresia, hypoplasia of pulmonary valve
See 746.995 if valve not specified;
e.g. "pulmonary atresia"
 - 746.010 Stenosis of pulmonary valve
See 746.995 if valve not specified;
e.g. "pulmonary stenosis"
Excludes: pulmonary infundibular
stenosis (use 746.830)
 - 746.020 Insufficiency of pulmonary valve
 - 746.080 Other specified anomalies of pulmonary valve
Excludes: pulmonary infundibular
stenosis (use 746.830)
 - 746.090 Unspecified anomaly of pulmonary valve
- 746.1 Tricuspid atresia and stenosis
 - 746.100 Tricuspid atresia, stenosis, hypoplasia
 - 746.105 Tricuspid insufficiency; excludes Ebstein's
- 746.2 Ebstein's anomaly
 - 746.200 Ebstein's anomaly
- 746.3 Congenital stenosis of aortic valve
 - 746.300 Congenital stenosis of aortic valve
Includes: congenital aortic stenosis
subvalvular aortic stenosis
Excludes: supravalvular aortic stenosis (747.220)
- 746.4 Congenital insufficiency of aortic valve
 - 746.400 Congenital insufficiency of aortic valve
bicuspid aortic valve
congenital aortic insufficiency
 - * 746.480 Other specified anomalies of the aortic valves
Includes: aortic valve atresia
Excludes: supravalvular aortic stenosis (747.220)
 - * 746.490 Unspecified anomalies of the aortic valves
- 746.5 Congenital mitral stenosis
 - 746.500 Congenital mitral stenosis
 - 746.505 Absence, atresia or hypoplasia of mitral valve
- 746.6 746.600 Congenital mitral insufficiency
- 746.7 746.700 Hypoplastic left heart syndrome
Atresia, or marked hypoplasia of the
ascending aorta and defective development
of left ventricle (with mitral valve atresia)

- 746.8 Other specified anomalies of the heart
- 746.800 Dextrocardia without situs inversus (situs solitus)
 Dextrocardia with no mention of situs inversus.
 Use 759.300 for dextrocardia with situs inversus.
- 746.810 Levocardia
- 746.820 Cor triatriatum
- 746.830 Pulmonary infundibular (subvalvular) stenosis
- 746.840 Trilogy of Fallot
- 746.850 Anomalies of pericardium
- # 746.860 Anomalies of myocardium
 Congenital cardiomegaly NOS
 Congenital myopathy
 Hypertrophic myopathy
- 746.870 Congenital heart block
- 746.880 Other specified anomalies of heart
 Includes:
 Ectopia (ectopic) cordis (Mesocordia)
 Conduction defects NOS
- 746.881 Hypoplastic left ventricle
 Excludes:
 Hypoplastic left heart syndrome(746.700)
- 746.882 Hypoplastic right heart (ventricle)
 Uhl's disease
- 746.885 Anomalies of coronary artery or sinus
- 746.886 Ventricular hypertrophy, (right or left)
- 746.887 Other defects of the atria
 Excludes:
 congenital Wolfe-Parkinson-White
 (use 426.705)
 rhythm anomalies (use 426.-, 427.-)
- 746.9 Unspecified anomalies of heart
- 746.900 Unspecified anomalies of heart valves
- 746.910 Anomalous bands of heart
- 746.920 Acyanotic congenital heart disease NOS
- 746.930 Cyanotic congenital heart disease NOS
 Blue baby
- # 746.990 Unspecified anomaly of heart:
 Includes:
 congenital heart disease (CHD)
 heart murmur
- 746.995 "Pulmonic" or "Pulmonary" atresia, stenosis, or
 hypoplasia NOS (no mention of valve or artery)

- 747 Other Congenital Anomalies of Circulatory System
- 747.000 Patent ductus arteriosus (PDA)
747.008 Probable PDA
- 747.1 Coarctation of aorta
- 747.100 Preductal (proximal) coarctation of aorta
747.110 Postductal (distal) coarctation of aorta
747.190 Unspecified coarctation of aorta
- 747.2 Other anomalies of aorta
- 747.200 Atresia of aorta
absence of aorta
pseudotruncus arteriosus
- 747.210 Hypoplasia of aorta
tubular hypoplasia of aorta
- 747.215 Interrupted aortic arch
- 747.220 Supra-aortic stenosis (supra-valvular)
Excludes:
aortic stenosis, congenital (See 746.300)
- 747.230 Persistent right aortic arch
- 747.240 Aneurysm of sinus of valsalva
- 747.250 Vascular ring (aorta)
double aortic arch
- 747.260 Overriding aorta
dextroposition of aorta
- 747.270 Congenital aneurysm of aorta
congenital dilatation of aorta
- 747.280 Other specified anomalies of aorta
- 747.290 Unspecified anomalies of aorta
- 747.3 Anomalies of pulmonary artery
- 747.300 Pulmonary artery atresia, absence or agenesis
Use 746.995 if artery or valve is not
specified
- 747.310 Pulmonary artery atresia with septal defect
- 747.320 Pulmonary artery stenosis
Use 746.995 if artery or valve is
not specified
- 747.325 Peripheral pulmonary artery stenosis
Includes:
peripheral pulmonic stenosis
- 747.330 Aneurysm of pulmonary artery
dilatation of pulmonary artery
- 747.340 Pulmonary arteriovenous malformation or aneurysm
- 747.380 Other specified anomaly of pulmonary artery
Includes:
pulmonary artery hypoplasia
- 747.390 Unspecified anomaly of pulmonary artery

- 747.4 Anomalies of great veins
 - 747.400 Stenosis of vena cava (inferior or superior)
 - 747.410 Persistent left superior vena cava
 - 747.420 (TAPVR) Total anomalous pulmonary venous return
 - 747.430 Partial anomalous pulmonary venous return
 - 747.440 Anomalous portal vein termination
 - 747.450 Portal vein - hepatic artery fistula
 - 747.480 Other specified anomalies of great veins
 - 747.490 Unspecified anomalies of great veins
- 747.5 Absence or hypoplasia of umbilical artery
 - # 747.500 Single umbilical artery
- 747.6 Other anomalies of peripheral vascular system
 - 747.600 Stenosis of renal artery
 - 747.610 Other anomalies of renal artery
 - 747.620 Arteriovenous malformation (peripheral)
 - Excludes: pulmonary (747.340)
 - cerebral (747.800)
 - retinal (743.510)
 - 747.630 Congenital phlebectasia
 - congenital varix
 - 747.640 Other anomalies of peripheral arteries
 - Includes: aberrant subclavian artery
 - 747.650 Other anomalies of peripheral veins
 - Excludes:
 - Budd-Chiari - occlusion of hepatic vein (use 453.000)
 - 747.680 Other anomalies of peripheral vascular system
 - Includes: primary pulmonary artery hypertension
 - 747.690 Unspecified anomalies of peripheral vascular sys
- 747.8 Other specified anomalies of circulatory system
 - 747.800 Arteriovenous (malformation)aneurysm of brain
 - 747.810 Other anomalies of cerebral vessels
 - Includes: vein of Galen
 - 747.880 Other specified anomalies of circulatory system
 - Excludes:
 - congenital aneurysm:
 - coronary (746.880)
 - peripheral (747.640)
 - pulmonary (747.330)
 - retinal (747.510)
 - ruptured cerebral arteriovenous aneurysm (430.000)
 - ruptured cerebral aneurysm (430.000)
- 747.9 747.900 Unspecified anomalies of circulatory system

748 Congenital Anomalies of Respiratory System

748.0 748.000 Choanal atresia
 atresia of nares, anterior or posterior
 congenital stenosis

748.1 Other anomalies of nose

 748.100 Agenesis or underdevelopment of nose

 748.110 Accessory nose

 748.120 Fissured, notched or cleft nose

 748.130 Sinus wall anomalies

 748.140 Perforated nasal septum

 # 748.180 Other specified anomalies of nose
 flat bridge of nose
 wide nasal bridge
 small nose and nostril
 absent nasal septum

 748.185 Tubular nose, single nostril, proboscis

 748.190 Unspecified anomalies of nose
 Excludes: congenital deviation of the nasal
 septum (use 754.020)

748.2 Web of larynx

 748.205 Web of larynx-glottic

 748.206 Web of larynx-subglottic

 748.209 Web of larynx-NOS

748.3 Other anomalies of larynx, trachea, and bronchus

 748.300 Anomalies of larynx and supporting cartilage

 748.310 Congenital subglottic stenosis

 # 748.320 Tracheomalacia

 748.330 Other anomalies of trachea

 748.340 Stenosis of bronchus

 748.350 Other anomalies of bronchus

 748.360 Congenital laryngeal stridor NOS

 748.380 Other specified anomalies of larynx and bronchus

 748.385 Cleft larynx, laryngo-tracheo-esophageal-cleft

 748.390 Unspecified anomalies of larynx, trachea and bronchus

748.4 Congenital cystic lung

 748.400 Single cyst, lung or lung cyst

 748.410 Multiple cysts, lung
 Polycystic lung

 748.420 Honeycomb lung

 748.480 Other specified congenital cystic lung

748.5 Agenesis or aplasia of lung

 748.500 Agenesis or aplasia of lung

 748.510 Hypoplasia of lung
 Pulmonary hypoplasia

 748.520 Sequestration of lung

 748.580 Other specified dysplasia of lung
 Fusion of lobes of lung

 *748.590 Unspecified dysplasia of lung

748.6 Other anomalies of lung

 748.600 Ectopic tissues in lung

 748.610 Bronchiectasis

 748.620 Accessory lobe of lung

 748.625 Bilobar right lung

 748.690 Other and unspecified anomalies of lung

748.8 Other specified anomalies of respiratory system

 748.800 Anomaly of pleura

 748.810 Congenital cyst of mediastinum

 748.880 Other specified respiratory system anomalies
 Includes: congenital lobar emphysema
 lymphangiectasia of lungs.

748.9 748.900 Unspecified anomalies of respiratory system
 Absence of respiratory organ NOS
 Anomaly of respiratory system NOS

749 Cleft Palate and Cleft Lip

749.0 Cleft palate alone
 (If description of condition includes Pierre Robin syndrome, use additional code, 524.080)

749.000 Cleft hard palate, unilateral
 749.010 Cleft hard palate, bilateral
 749.020 Cleft hard palate, central
 749.030 Cleft hard palate NOS
 749.040 Cleft soft palate, alone unilateral
 749.050 Cleft soft palate, alone bilateral
 749.060 Cleft soft palate, alone central
 749.070 Cleft soft palate, alone NOS
 749.080 Cleft uvula
 749.090 Cleft palate NOS
 palatoschisis

749.1 Cleft lip alone
 Includes:
 alveolar ridge cleft
 cleft gum
 harelip

749.100 Cleft lip, unilateral
 749.110 Cleft lip, bilateral
 749.120 Cleft lip, central
 749.190 Cleft lip NOS (fused lip)
 Cleft gum

749.2 Cleft lip with cleft palate

749.200 Cleft lip, unilateral, with cleft palate (any)
 749.210 Cleft lip, bilateral, with cleft palate (any)
 749.220 Cleft lip, central, with cleft palate (any)
 749.290 Cleft lip NOS, with any cleft palate

- 750 Other Congenital Anomalies of Upper Alimentary Tract
- # 750.000 Tongue tie
Ankyloglossia
- 750.1 Other anomalies of tongue
- 750.100 Aglossia
Absence of tongue
- 750.110 Hypoglossia of tongue (small tongue)
Microglossia
- 750.120 Macroglossia (large tongue)
- 750.130 Dislocation or displacement of tongue
(glossoptosis)
- 750.140 Cleft tongue (split)
- 750.180 Other specified anomalies of tongue
- 750.190 Unspecified anomalies of tongue
- 750.2 Other specified anomalies of mouth and pharynx
- 750.200 Pharyngeal pouch
- 750.210 Other pharyngeal anomalies
- 750.220 Ranula
Includes: mucoceles of soft palate,
epulis
- 750.230 Other anomalies of salivary glands or ducts
- 750.240 High arched palate
- 750.250 Other anomalies of palate
- 750.260 Lip fistulae or pits
- 750.270 Other lip anomalies
prominent philtrum, long philtrum
- 750.280 Other specified anomalies of mouth and pharynx
Excludes: receding jaw (see 524.000)
large and small mouth (see 744.800)
- 750.3 Tracheo-esophageal fistula (T-E), esophageal atresia and stenosis
- 750.300 Esophageal atresia without mention of (T-E) fistula
- 750.310 Esophageal atresia with mention of (T-E) fistula
- 750.320 Tracheo-esophageal (T-E) fistula without mention of esophageal atresia
- 750.325 Tracheo-esophageal fistula - "H" type
- 750.330 Broncho-esophageal fistula with or without mention of esophageal atresia
- 750.340 Stenosis or stricture of esophagus
- 750.350 Esophageal web
- 750.380 Other tracheo-esophageal anomalies

- 750.4 Other specified anomalies of esophagus
 - 750.400 Congenital dilatation of esophagus
 - Giant esophagus
 - 750.410 Displacement of esophagus
 - 750.420 Diverticulum of esophagus
 - esophageal pouch
 - 750.430 Duplication of esophagus
 - 750.480 Other specified anomalies of esophagus

- 750.5 Congenital hypertrophic pyloric stenosis
 - # 750.500 Pylorospasm
 - 750.510 Congenital hypertrophic pyloric stenosis
 - 750.580 Other congenital pyloric obstruction

- 750.6 750.600 Congenital hiatus hernia
 - Cardia displacement through esophageal hiatus
 - Partial thoracic stomach
 - Excludes:
 - congenital diaphragmatic hernia (756.610)

- 750.7 Other specified anomalies of stomach
 - 750.700 Microgastria
 - 750.710 Megalogastrica
 - 750.720 Cardiospasm
 - achalasia of cardia, congenital
 - 750.730 Displacement or transposition of stomach
 - 750.740 Diverticulum of stomach
 - 750.750 Duplication of stomach
 - 750.780 Other specified anomalies of stomach

- 750.8 750.800 Other specified anomalies of upper alimentary tract

- 750.9 Unspecified anomalies of upper alimentary tract
 - 750.900 Unspecified anomalies of mouth and pharynx
 - 750.910 Unspecified anomalies of esophagus
 - 750.920 Unspecified anomalies of stomach
 - 750.990 Unspecified anomalies of upper alimentary tract

- 751 Other Congenital Anomalies of Digestive System
- 751.0 Meckel's diverticulum
 - 751.000 Persistent omphalomesenteric duct
persistent vitelline duct
 - * 751.010 Meckel's diverticulum
- 751.1 Atresia and stenosis of small intestine
 - 751.100 Stenosis, atresia or absence of duodenum
 - 751.110 Stenosis, atresia or absence of jejunum
 - 751.120 Stenosis, atresia or absence of ileum
 - 751.190 Stenosis, atresia or absence of small intestine
 - 751.195 Stenosis, atresia or absence of small intestine
with fistula
- 751.2 Atresia and stenosis of large intestine, rectum
and anal canal
 - 751.200 Stenosis, atresia or absence of large intestine
Stenosis, atresia or absence of appendix
 - 751.210 Stenosis, atresia or absence of rectum with fistula
 - 751.220 Stenosis, atresia or absence of rectum without
mention of fistula
 - 751.230 Stenosis, atresia or absence of anus with fistula
Includes: "imperforate anus" with fistula
 - 751.240 Stenosis, atresia or absence of anus without
mention of fistula.
Includes: "imperforate anus" without fistula
- 751.3 Hirschsprung's disease and other congenital
functional disorders of the colon
 - 751.300 Total intestinal aganglioneosis
 - 751.310 Long-segment Hirschsprung's disease
 - 751.320 Short-segment Hirschsprung's disease
 - 751.330 Hirschsprung's disease NOS
 - 751.340 Congenital megacolon
congenital macrocolon, not aganglionic

- 751.4 Anomalies of intestinal fixation
 - 751.400 Malrotation of caecum and/or colon
 - 751.410 Anomalies of mesentery
 - 751.420 Congenital adhesions or bands of omentum and peritoneum
 - 751.490 Other specified and unspecified malrotation
 - 751.495 Malrotation of small intestine alone

- 751.5 Other anomalies of intestine
 - 751.500 Duplication of anus, appendix, caecum or intestine enterogenous cyst
 - 751.510 Transposition of appendix, colon or intestine
 - 751.520 Microcolon
 - 751.530 Ectopic (displaced) anus
 - 751.540 Congenital anal fistula
 - 751.550 Persistent cloaca
 - # 751.580 Other specified anomalies of intestine
 - 751.590 Unspecified anomalies of intestine

- 751.6 Anomalies of gallbladder, bile ducts and liver
 - 751.600 Absence or agenesis of liver, total or partial
 - 751.610 Cystic or fibrocystic disease of liver
 - # 751.620 Other anomalies of liver
 - hepatomegaly
 - hepatosplenomegaly also use code 759.020
 - Excludes:
 - Budd Chiari (use 453.000)
 - 751.630 Agenesis or hypoplasia of gallbladder
 - 751.640 Other anomalies of gallbladder
 - duplication of gallbladder
 - 751.650 Agenesis or atresia of hepatic or bile ducts
 - Includes:
 - biliary atresia
 - Excludes:
 - congenital or neonatal hepatitis (use 774.480 or 774.490)
 - 751.660 Choledochal cysts
 - 751.670 Other anomalies of hepatic or bile ducts
 - 751.680 Anomalies of biliary tract, NEC

751.7 Anomalies of pancreas
 Excludes:
 diabetes mellitus:
 congenital (250.000)
 neonatal (775.100)
 fibrocystic disease of pancreas (277.000)

751.700 Absence, agenesis or hypoplasia of pancreas
 751.710 Accessory pancreas
 751.720 Annular pancreas
 751.730 Ectopic pancreas
 751.740 Pancreatic cyst
 751.780 Other specified anomalies of pancreas
 751.790 Unspecified anomalies of pancreas

751.8 Other specified anomalies of digestive system

751.800 Absence of alimentary tract NOS
 (complete or partial)
 751.810 Duplication of alimentary tract
 751.820 Ectopic digestive organs NOS
 751.880 Other specified anomalies of digestive system

751.9

751.900 Unspecified anomalies of digestive system
 congenital of digestive system NOS:
 anomaly NOS
 deformity NOS
 obstruction NOS

- 752 Congenital Anomalies of Genital Organs
 Excludes:
 congenital hydrocele (778.600)
 testicular feminization syndrome (257.800)
 syndromes associated with anomalies in number
 and form of chromosomes (758.---)
- 752.0 Anomalies of ovaries
- 752.000 Absence or agenesis of ovaries
 752.010 Streak ovary
 752.020 Accessory ovary
 752.080 Other specified anom of ovaries
 752.085 Multiple ovarian cysts
 752.090 Unspecified anomalies of ovaries
- 752.1 Anomalies of fallopian tubes and broad ligaments
- 752.100 Absence of fallopian tube or broad ligament
 752.110 Cyst of mesenteric remnant
 epoochoron cyst
 cyst of Gartner's duct
 752.120 Fimbrial cyst
 parovarian cyst
 752.190 Other and unspecified anomalies of fallopian tube
 and broad ligaments
- 752.2 752.200 Doubling of uterus
 doubling of uterus (any degree) or
 associated with doubling of cervix and
 vagina

- 752.3 Other anomalies of uterus
- 752.300 Absence or agenesis of uterus
- 752.310 Displaced uterus
- 752.320 Fistulae involving uterus with digestive or
 urinary tract
 uterointestinal fistula
 uterovesical fistula
- 752.380 Other anomalies of uterus
 bicornuate uterus
 unicornous uterus
- 752.390 Unspecified anomalies of uterus
- 752.4 Anomalies of cervix, vagina and external female
 genitalia
- 752.400 Absence, atresia or agenesis of cervix
- 752.410 Absence or atresia of vagina—complete or partial
- 752.420 Congenital rectovaginal fistula
- 752.430 Imperforate hymen
- 752.440 Absence or other anomaly of vulva
 fusion of vulva
 hypoplastic labia majora
- 752.450 Absence or other anomaly of clitoris
 Includes:
 clitoromegaly
 enlarged clitoris
 clitoral hypertrophy
- # 752.460 Embryonal cyst of vagina
- 752.470 Other cyst of vagina, vulva or canal of Nuck
- # 752.480 Other specified anomalies of cervix, vagina or
 external female genitalia
 Includes: vaginal tags
 hymenal tags
- # 752.490 Unspecified anomalies of cervix, vagina or
 external female genitalia

752.5 Undescended testicle
 Not coded if < 2500 gms
 Excludes: retractile testicle (V65.50)

752.500 Undescended testicle, unilateral
 undescended unpalpable

752.501 Left undescended testicle

752.502 Right undescended testicle

752.514 Undescended testicle, bilateral

752.520 Undescended testicle NOS

752.530 Ectopic testis, unilateral and bilateral

752.6 Hypospadias and epispadias

752.600 Hypospadias (alone) NOS.

752.605 1⁰, glandular, coronal

752.606 2⁰, penile,

752.607 3⁰, perineal, scrotal

752.610 Epispadias

752.620 Congenital chordee (with hypospadias), NOS

752.621 Congenital chordee alone (chordee w/o hypospadias)

752.625 Cong. chordee with 1⁰, coronal hypospadias

752.626 Cong. chordee with 2⁰, penile hypospadias

752.627 Cong. chordee with 3⁰, perineal, scrotal hypospadias

752.7 Indeterminate sex and pseudohermaphroditism
 Excludes: pseudohermaphroditism:
 female, with adrenocortical disorder
 (see 255.200)
 male, with gonadal disorder (257.900)
 with specified chromosomal anomaly (758.000)

752.700 True hermaphroditism
 ovotestis

752.710 Pseudohermaphroditism, male

752.720 Pseudohermaphroditism, female
 pure gonadal dysgenesis
 Excludes: gonadal agenesis (758.690)

752.730 Pseudohermaphrodite NOS

752.790 Indeterminate sex NOS
 ambiguous genitalia

- 752.8 Other specified anomalies of male genital organs
- 752.800 Absence of testis
 monorchidism NOS
- # 752.810 Aplasia or hypoplasia of testis and scrotum
- 752.820 Other anomalies of testis and scrotum
 polyorchidism
 bifid scrotum
- 752.830 Atresia of vas deferens
- 752.840 Other anomalies of vas deferens and prostate
- 752.850 Absence or aplasia of penis
- 752.860 Other anomalies of penis
 absent, hooded, or redundant foreskin
- 752.865 Small (micro) penis or hypoplastic penis
- 752.870 Cysts of embryonic remnants
 cyst: hydatid of Morgagni
 Wolffian duct
 Appendix testis
- 752.880 Other specified anomalies of genital organs
 microgenitalia
 macrogenitalia
- 752.9 752.900 Unspecified anomalies of genital organs
 Congenital: of genital organ, NEC
 Anomaly NOS or deformity NOS

- 753 Congenital Anomalies of Urinary System
- 753.0 Renal agenesis and dysgenesis
 - 753.000 Bilateral absence, agenesis, dysplasia, or hypoplasia of kidneys
 - Potter's syndrome
 - 753.009 Renal agenesis NOS
 - 753.010 Unilateral absence, agenesis, dysplasia or hypoplasia of kidneys
- 753.1 Cystic kidney disease
 - 753.100 Renal cyst (single)
 - 753.110 Polycystic kidneys, infantile type
 - 753.120 Polycystic kidneys, adult type
 - 753.130 Polycystic kidneys NOS
 - 753.140 Medullary cystic disease, juvenile type
 - 753.150 Medullary cystic disease, adult type
 - Medullary sponge kidney
 - 753.160 Multicystic renal dysplasia
 - Multicystic kidney
 - 753.180 Other specified cystic disease
 - Includes: cystic kidneys, NOS
- 753.2 Obstructive defects of renal pelvis and ureter
 - 753.200 Congenital hydronephrosis
 - 753.210 Atresia, stricture, or stenosis of ureter
 - Includes:
 - Ureteropelvic junction obstruction/stenosis
 - Ureterovesical junc. obstruction/stenosis
 - Hypoplastic ureter
 - 753.220 Megaloureter NOS
 - Includes: hydroureter
 - 753.290 Other and unspecified obstructive defects of renal pelvis and ureter
- 753.3 Other specified anomalies of kidney
 - 753.300 Accessory kidney
 - 753.310 Double or triple kidney and pelvis
 - Pyelon duplex or triplex
 - 753.320 Lobulated, fused or horseshoe kidney
 - 753.330 Ectopic kidney
 - 753.340 Enlarged, hyperplastic or giant kidney
 - 753.350 Congenital renal calculi
 - 753.380 Other specified anomalies of kidney

- 753.4 Other specified anomalies of ureter
 - 753.400 Absence of ureter
 - 753.410 Accessory ureter
 - double ureter
 - 753.420 Ectopic ureter
 - 753.480 Other specified anomalies of ureter
 - Includes: ureterocele
 - 753.485 Variations of vesico-ureteral reflux
- 753.5 753.500 Exstrophy of urinary bladder
 - ectopia vesicae
 - extroversion of bladder
- 753.6 Atresia and stenosis of urethra and bladder neck
 - 753.600 Cong. posterior urethral valves or posterior
 - urethral obstruction
 - 753.610 Other atresia, or stenosis of bladder-neck
 - 753.620 Obstruction, atresia or stenosis of anterior
 - urethra
 - 753.630 Obstruction, atresia or stenosis of urinary meatus
 - Includes: meatal stenosis
 - 753.690 Other and unspecified atresia and stenosis of urethra
 - and bladder neck
- 753.7 Anomalies of urachus
 - 753.700 Patent urachus
 - 753.710 Cyst of urachus
 - 753.790 Other and unspecified anomaly of urachus
- 753.8 Other specified anomalies of bladder and urethra
 - 753.800 Absence of bladder or urethra
 - 753.810 Ectopic bladder
 - 753.820 Congenital diverticulum or hernia of bladder
 - 753.830 Congenital prolapse of bladder (mucosa)
 - 753.840 Double urethra or urinary meatus
 - 753.850 Ectopic urethra or urethral orifice
 - 753.860 Congenital digestive-urinary tract fistulae
 - rectovesical fistula
 - 753.870 Urethral fistula NOS
 - 753.880 Other specified anomalies of bladder and urethra
- 753.9 Unspecified anomalies of urinary system
 - 753.900 Unspecified anomaly of kidney
 - 753.910 Unspecified anomaly of ureter
 - 753.920 Unspecified anomaly of bladder
 - 753.930 Unspecified anomaly of urethra
 - 753.990 Unspecified anomaly of urinary system NOS

- 754 Certain Congenital Musculoskeletal Deformities
- 754.0 Of skull, face and jaw
- Excludes:
- dentofacial anomalies (524.000)
 - Pierre Robin syndrome (524.080)
 - syphilitic saddle nose (090.000)
- 754.000 Asymmetry of face
- 754.010 Compression (Potter's) facies
- 754.020 Congenital deviation of nasal septum
bent nose
- 754.030 Dolichocephaly
- # 754.040 Depressions in skull
- Includes: large fontanelle
small fontanelle
- 754.050 Plagiocephaly
- 754.055 Asymmetric head
- * 754.060 Scaphocephaly, no mention of craniosynostosis
- * 754.070 Trigocephaly, no mention of craniosynostosis
- * 754.080 Other specified skull deformity, no mention of
craniosynostosis
- Includes:
- brachycephaly
 - acrocephaly
 - turriccephaly
 - oxycephaly
- * 754.090 Deformity of skull (NOS)
- 754.1
- 754.100 Of sternocleidomastoid muscle
- Includes:
- * absent or hypoplastic sternocleidomastoid
contracture of sternocleidomastoid (muscle)
sternomastoid tumor
- Excludes:
- congenital sternocleidomastoid torticollis
(use 756.860)
- 754.2 Certain congenital musculoskeletal deformities
of spine
- 754.200 Congenital postural scoliosis
- 754.210 Congenital postural lordosis
- 754.220 Congenital postural curvature of spine, NOS
- 754.3 Congenital dislocation of hip
- 754.300 Congenital dislocation of hip
- 754.310 Unstable hip
- preluxation of hip
 - subluxation of hip
 - predislocation status of hip at birth
- # 754.320 Clicking hip

- 754.4 Congenital genu recurvatum and bowing of long bones of leg
- 754.400 Bowing, femur
- 754.410 Bowing, tibia and/or fibula
- 754.420 Bow legs NOS
- 754.430 Genu recurvatum
- 754.440 Dislocation of knee, congenital
- 754.490 Deformity of leg NOS
- 754.5 Varus (inward) deformities of feet
- 754.500 Talipes equinovarus
- 754.510 Talipes calcaneovarus
- 754.520 Metatarsus varus
- 754.530 Complex varus deformities
- 754.590 Unspecified varus deformities of feet
- 754.6 Valgus (outward) deformities of feet
- 754.600 Talipes calcaneovalgus
- 754.610 Congenital pes planus
- 754.615 Pes valgus
- 754.680 Other specified valgus deformities of foot
- 754.690 Unspecified valgus deformities of foot
- 754.7 Other deformities of feet
- 754.700 Pes cavus
- Claw foot (use 753.350 for claw foot)
- 754.720 Short Achilles tendon
- 754.730 Clubfoot NOS
- talipes NOS
- 754.735 Congenital deformities of foot NOS
- 754.780 Other specified deformities of ankle and/or toes
- Includes:
- dorsiflexion of foot
- widely spaced toes
- 754.8 Other specified congenital musculoskeletal deformities
- 754.800 Pigeon chest (Pectus Carinatum)
- 754.810 Funnel chest (Pectus Excavatum)
- 754.820 Other anomalies of chest wall
- Includes: 'deformed chest', barrel chest
- 754.825 Shield chest
- 754.830 Dislocation of elbow
- 754.840 Club hand or fingers
- 754.850 Spade-like hand
- 754.880 Other specified deform. of hands
- See 755.500 for specified anomalies of fingers, eg. incurving fingers

755 Other Congenital Anomalies of Limbs

755.0 Polydactyly

755.005 Accessory fingers, (postaxial polydactyly)
(Type A)

755.006 Skin tag, (postaxial polydactyly)
(Type B)

755.007 Unspecified finger or skin tag (postaxial
polydactyly NOS)

755.010 Accessory thumbs, (preaxial polydactyly)

755.020 Accessory toes (postaxial)

755.030 Accessory big toe (preaxial)

755.090 Accessory digits NOS (hand/foot not specified)

755.095 Accessory digits hand NOS (pre-, postaxial not
specified)

755.096 Accessory digits foot NOS (pre-, postaxial not
specified)

755.1 Syndactyly

755.100 Fused fingers

755.110 Webbed fingers

755.120 Fused toes

755.130 Webbed toes

755.190 Unspecified syndactyly (see below for specified site)

755.191 Unspecified syndactyly thumb and/or fingers
unilateral

755.192 Unspecified syndactyly thumb and/or fingers
bilateral

755.193 Unspecified (webbed vs fused) syndactyly thumb
and/or fingers NOS

755.194 Unspecified syndactyly toes unilateral

755.195 Unspecified syndactyly toes bilateral

755.196 Unspecified syndactyly toes NOS

755.199 Unspecified syndactyly (i.e., webbed vs fused)
digits not known

- 755.2 Reduction defects of upper limb
 If description of condition includes amniotic or
 constricting bands use additional code, 658.800
- 755.200 Complete absence of upper limb
 amelia of upper limb
- 755.210 Absence of upper arm and forearm with hand present
 phocomelia of upper limb
- 755.220 Absence of forearm only (radius and ulna)
- 755.230 Absence of forearm and hand
- 755.240 Absence of hand and/or fingers
 Excludes:
 hypoplasia of upper limb (use 755.585)
- 755.250 Lobster claw hand
 Excludes:
 shortening of arm (use 755.580)
- 755.260 Preaxial (longitudinal) reduction defects of upper limb
 Includes:
 absence of radius
 absence of thumb
- 755.270 Postaxial (longitudinal) reduction defects of upper
 limb
 Includes:
 absence of ulna
 absence of fingers
- 755.280 Other specified upper limb reduction defects
- 755.290 Unspecified reduction defect of upper limb
 Includes:
 congenital amputation of upper limb NOS
- 755.3 Reduction defects of lower limb
 If description of condition includes amniotic or
 constricting bands use additional code, 658.800
- 755.300 Complete absence of lower limb
 amelia of lower limb
- 755.310 Absence of thigh and lower leg with foot present
 phocomelia of lower limb
- 755.320 Absence of lower leg only
- 755.330 Absence of lower leg and foot
- 755.340 Absence of foot or toes
 Excludes:
 hypoplasia of lower limb (use 755.685)
- 755.350 Claw foot or Lobster claw foot
 Excludes:
 shortening of leg (use 755.680)
- 755.360 Longitudinal reduction defect of leg, NOS
- 755.365 Absent tibia (preaxial longitudinal defect)
- 755.366 Absent fibula (postaxial longitudinal defect)
- 755.380 Other Specified reduction defect of lower limb
 Includes:
 absent upper leg or thigh only
- 755.390 Unspecified reduction defect of lower limb
 Includes:
 congenital amputation of lower limb NOS

- 755.4 Reduction defects, unspecified limb
 If description of condition includes amniotic or
 constricting bands use additional code, 658.800
- 755.400 Absence limb NOS
 amelia NOS
- 755.410 Phocomelia NOS
- 755.420 Amputation of unspecified limb
- 755.430 Longitudinal reduction defect NOS
- 755.440 Absent digits NOS
- 755.480 Other specified reduction defect of unspecified limb
- 755.490 Unspecified reduction defect of unspecified limb
- 755.5 Other anomalies of upper limb, including shoulder
 girdle
 Includes:
 complex anomalies involving all or part of
 upper limb
- # 755.500 Anomalies of fingers
 Includes:
 Camptodactyly Clinodactyly
 Macroductyilia Brachydactyly
 Triphalangeal thumb Incurving fingers
 Acrocephalosyndactyly (see 756.050)
 Apert's syndrome (see 756.055)
- 755.510 Anomalies of hand
 Excludes: 'simian crease' (use 757.200)
- 755.520 Anomalies of wrist
- 755.525 Accessory carpal bones
- 755.526 Madelung's deformity
- 755.530 Anomalies of forearm, NOS
- 755.535 Radio-ulnar dysostosis
- 755.536 Radio-ulnar synostosis
- 755.540 Anomalies of elbow and upper arm
- 755.550 Anomalies of shoulder
- 755.555 Cleidocranial dysostosis
- 755.556 Sprengel's deformity
- 755.560 Other anomalies of whole arm
- 755.580 Other specified anomalies of upper limb
 Includes:
 hyperextensibility of upper limb
 shortening of arm
- 755.585 Hypoplasia of upper limb
 Includes:
 hypoplasia of fingers, hands, or arms
 Excludes:
 aplasia or absent upper limb (see 755.2__)
- 755.590 Unspecified anomalies of upper limb

755.6

Other anomalies of lower limb, including pelvic girdle

Includes: complex anomalies involving all or part of lower limb

755.600 Anomalies of toes

Includes:

overlapping toes hammer toes
widespaced 1st and 2nd toes

755.605 Hallux valgus

755.606 Hallux varus

755.610 Anomalies of foot

Includes:

plantar furrow

Excludes:

lobster claw foot (use 755.350)

755.616 Rocker bottom foot

755.620 Anomalies of ankle

Astragaloscaphoid synostosis

755.630 Anomalies of lower leg

Angulation of tibia, tibial torsion
(exclude if clubfoot present)

755.640 Anomalies of knee

hyperextended knee

755.645 Genu valgum

755.646 Genu varum

755.647 Absent patella or rudimentary patella

755.650 Anomalies of upper leg

Anteversión of femur

755.660 Anomalies of hip

Includes: coxa vara

coxa valga

other abnormalities of hips

755.665 Hip dysplasia, NOS

755.666 Unilateral hip dysplasia

755.667 Bilateral hip dysplasia

755.670 Anomalies of pelvis

fusion of sacroiliac joint

755.680 Other specified anom. of lower limb

hyperextended legs

shortening of legs

755.685 Hypoplasia of lower limb

Includes:

hypoplasia of toes, feet, legs

Excludes:

aplasia or absent lower limb (see 755.3__)

755.690 Unspecified anomalies of legs

755.8 Other specified anomalies of unspecified limb

755.800 Arthrogryposis multiplex congenita
 Temporarily includes—flexion contractures
 of individual joints

755.810 Larsen's syndrome

755.880 Other specified anomalies of unspecified limb
 Includes:
 overlapping digits NOS
 hyperextended joints NOS
 Excludes:
 hyperextended knees (use 755.640)

755.9 755.900 Unspecified anomalies of unspecified limb

756 Other Congenital Musculo-Skeletal Anomalies

756 Other Congenital Musculo-Skeletal Anomalies

- 756.0 Anomalies of skull and face bones
Excludes:
skull and face deformities in 754.____
Pierre Robin syndrome (use 524.080)
- 756.000 Craniosynostosis, NOS
craniostenosis, NOS
closed skull sutures, NOS
- 756.005 Sagittal craniosynostosis
- 756.006 Metopic craniosynostosis
- 756.010 Coronal craniosynostosis
- 756.020 Lambdoidal craniosynostosis
- 756.030 Other types of craniosynostosis
Includes: Basilar craniosynostosis
- 756.040 Craniofacial dysostosis
Includes: Crouzon's disease
- 756.045 Mandibulofacial dysostosis
Includes: Franceschetti syndrome
Treacher-Collins syndrome
- 756.046 Other craniofacial syndromes
Includes: Oculomandibulofacial syndrome
Hallerman-Streif syndrome
- 756.050 Acrocephalosyndactyly, NOS
- 756.055 Acrocephalosyndactyly types I or II
Apert syndrome
- 756.056 Acrocephalosyndactyly type III
- 756.057 Other Specified Acrocephalosyndactylies
- 756.060 Goldenhar's syndrome
oculo-auriculo-vertebral dysplasia
- 756.065 Hemifacial macrosomia
- 756.080 Other specified skull and face bone anomalies
Includes:
localized skull defects
flat occiput
prominent occiput
prominent maxilla
Excludes:
macrocephaly (use 742.400)
small chin (use 524.000)
Pierre Robin syndrome (use 524.080)
- 756.085 Hypertelorism, telecanthus
- 756.090 Unspecified skull and face bone anomalies
Excludes:
dentofacial anomalies (524.000)
skull defects associated with brain anomalies such as:
Anencephalus (740.020)
Encephalocele (742.000)
Hydrocephalus (743.200)
Microcephalus (742.100)

- 756.1 Anomalies of spine
- 756.100 Spina bifida occulta
- 756.110 Klippel-Feil syndrome
 Wildervanck's syndrome
- 756.120 Kyphosis
 kyphoscoliosis
- 756.130 Congenital spondylolisthesis
- 756.140 Anomalies of cervical vertebrae
- 756.145 Hemivertebrae (cervical)
- 756.146 Agenesis (cervical)
- 756.150 Anomalies of thoracic vertebrae
- 756.155 Hemivertebrae of thoracic vertebrae
- 756.156 Agenesis of thoracic vertebrae
- 756.160 Anomalies of lumbar vertebrae
- 756.165 Hemivertebrae of lumbar vertebrae
- 756.166 Agenesis of lumbar vertebrae
- 756.170 Sacrococcygeal anomalies
 Includes: agenesis of sacrum
 Excludes: pilonidal sinus (see 685.100)
- 756.179 Sacral mass, NOS
- 756.180 Other specified vertebral anomalies
- 756.185 Hemivertebrae NOS
- 756.190 Unspecified anomalies of spine
- 756.2
- # 756.200 Cervical rib
 supernumerary rib in cervical region
- 756.3 Other anomalies of ribs and sternum
- 756.300 Absence of ribs
- 756.310 Misshapen ribs
- 756.320 Fused ribs
- 756.330 Extra ribs
- 756.340 Other anomalies of ribs
- 756.350 Absence of sternum
- 756.360 Misshapen sternum
- 756.380 Other anomalies of sternum
 bifid sternum, short sternum
- 756.390 Anomalies thoracic cage, unspecified
 Excludes: deformed chest (see 754.820)

756.4

Chondrodystrophy

- 756.400 Asphyxiating thoracic dystrophy
 - Jeune's syndrome
 - Thoracic-pelvic-phalangeal dysplasia
 - Excludes: homozygous achondroplasia
- 756.410 Chondrodysplasia
 - Oilier's syndrome, enchondromatosis
- 756.420 Chondrodysplasia with haemangioma
 - Kast's syndrome
 - Maffucci's syndrome
- 756.430 Achondroplastic dwarfism
- 756.440 Other specified chondrodystrophies
 - Excludes: Conradi's (see 756.575)
- 756.445 Diastrophic dwarfism
- 756.446 Metatrophic dwarfism
- 756.447 Thanatophoric dwarfism
- 756.450 Metaphyseal dysostosis
- 756.460 Spondyloepiphyseal dysplasia
- 756.470 Exostosis
 - Excludes: Gardner's syndrome (see 759.63_)
- 756.480 Other specified chondrodystrophy
- 756.490 Unspecified chondrodystrophy
 - Excludes: lipochondrodystrophy (see 277.59_)

756.5

Osteodystrophies

- 756.500 Osteogenesis imperfecta
- 756.505 Osteosathrosis
- 756.506 Fragilitas ossium
- 756.510 Polyostotic fibrous dysplasia
 - Albright-McCune-Sternberg syndrome
- 756.520 Chondroectodermal dysplasia
- 756.525 Ellis-van Creveld syndrome
- 756.530 Infantile cortical hyperostosis
 - Caffey's syndrome
- 756.540 Osteopetrosis
 - Albers-Schonberg syndrome
 - Marble bones
- 756.550 Progressive diaphyseal dysplasia
 - Engelmann's syndrome
 - Camurati-Englemann disease
- 756.560 Osteopoikilosis
- 756.570 Multiple epiphyseal dysplasia
- 756.575 Conradi's syndrome
 - Chondrodysplasia punctata
 - Excludes: warfarin embryopathy
- 756.580 Other specified osteodystrophies
- 756.590 Unspecified osteodystrophies

- 756.6 Anomalies of diaphragm
- 756.600 Absence of diaphragm
 - 756.610 Congenital diaphragmatic hernia
 - 756.615 Diaphragmatic hernia (Bochdalek)
 - 756.616 Diaphragmatic hernia (Morgagni)
 - 756.617 Hemidiaphragm
 - 756.620 Eventration of diaphragm
 - 756.680 Other specified anomalies of diaphragm
 - 756.690 Unspecified anomalies of diaphragm
- 756.7 Anomalies of abdominal wall
- 756.700 Exomphalos-omphalocele
 - 756.710 Gastroschisis
 - Excludes: umbilical hernia (553.100)
 - 756.720 Prune belly syndrome
 - # 756.790 Other and unspecified anom of abdominal wall
 - 756.795 Epigastric hernia
- 756.8 Other specified anomalies of muscle, tendon,
fascia and connective tissue
- 756.800 Poland's syndrome or anomaly
 - 756.810 Other absent or hypoplastic muscle
 - Includes:
 - absent pectoralis major
 - Excludes:
 - prune belly syndrome (use 756.720)
 - 756.820 Absent tendon
 - 756.830 Nail-patella syndrome
 - 756.840 Amyotrophia congenita
 - 756.850 Ehlers-Danlos syndrome
 - 756.860 Congenital torticollis
 - See also 754.100 Deformities of Sternocleido-
mastoid muscle.
 - 756.880 Other specified anomalies of muscle, tendon, fascia
and connective tissue
- 756.9 Unspecified anomalies of musculoskeletal system
- 756.900 Unspecified anomalies of muscle
 - 756.910 Unspecified anomalies of tendon
 - 756.920 Unspecified anomalies of bones
 - 756.930 Unspecified anomalies of cartilage
 - 756.940 Unspecified anomalies of connective tissue
 - 756.990 Unspecified anomalies of musculoskeletal system

- 757 Congenital Anomalies of the Integument
- 757.000 Hereditary oedema of legs
Hereditary trophoedema
Milroy's disease
- 757.1 Ichthyosis congenita
- 757.100 Harlequin fetus
- 757.110 Collodion baby
- 757.115 Bullous type
- 757.120 Sjogren-Larsson syndrome
- 757.190 Other and unspecified
- 757.195 Ichthyosis vulgaris
- 757.196 X-linked ichthyosis
- 757.197 Ichthysiform erythroderma
- 757.2 Dermatoglyphic anomalies
- # 757.200 Abnormal palmar creases
Includes:
simian creases, transverse palmar creases
- 757.3 Other specified anomalies of skin
Excludes: pigmented mole (216.900)
hemangioma (228.000)
- 757.300 Specified syndromes, not elsewhere classified,
involving skin anomalies
- # 757.310 Skin tags
Includes: anal tags
Excludes: preauricular tag (see 744.110)
vaginal tags (see 752.480)
- 757.320 Urticaria pigmentosa
- 757.330 Epidermolysis bullosa
- 757.340 Ectodermal dysplasia
Excludes: Ellis-van Créveld syndrome (756.525)
- 757.345 X-linked type ectodermal dysplasia
- 757.346 Other specified ectodermal dysplasias
- 757.350 Incontinentia pigmenti
- 757.360 Xeroderma pigmentosum
- 757.370 Cutis laxa hyperelastica
- # 757.380 Nevus, not elsewhere classifiable
Includes: port wine stain or nevus flammeus
Excludes: hairy naevus (use 216.900)
Sturge-Weber syndrome (use 759.610)
- # 757.385 Birthmark NOS
- # 757.386 Mongolian blue spot
- # 757.390 Other specified anomalies of skin
Includes: cafe au lait spots
hyperpigmented areas
skin cysts
- 757.395 Absence of skin

- 757.4 Specified anomalies of hair
Excludes: kinky hair syndrome (759.870)
- 757.400 Congenital alopecia
Excludes: ectodermal dysplasia (757.340)
- 757.410 Beaded hair
Monilethrix
- 757.420 Twisted hair
Pili torti
- 757.430 Taenzer's hair
- 757.450 Persistent or excessive lanugo
Includes: Hirsutism
- 757.480 Other spec anomalies of hair
- 757.5 Specified anomalies of nails
- 757.500 Congenital anonychia
Absent nails
- 757.510 Enlarged or hypertrophic nails
- 757.515 Onychauxis
- 757.516 Pachyonychia
- 757.520 Congenital koilonychia
- 757.530 Congenital leukonychia
- 757.540 Club nail
- 757.580 Other spec anomalies of nails
- 757.585 Hypoplastic (small) fingernails and/or toenails
- 757.6 Specified anomalies of breast
- 757.600 Absent breast with absent nipple
- 757.610 Hypoplastic breast with hypoplastic nipple
- 757.620 Accessory (ectopic) breast with nipple
- 757.630 Absent nipple
- 757.640 Small nipple (hypoplastic)
- * 757.650 Accessory (ectopic) nipple, supernumerary
- * 757.680 Other specified anomalies of breast
Widely spaced nipples
- 757.8 Other specified anomalies of the integument
- 757.800 Includes: scalp defects
For specified anomalies of skin see 757.390
For specified anomalies of hair see 757.480
For specified anomalies of nails see 757.580
- 757.9 Unspecified anomalies of the integument
- 757.900 Unspecified anomalies of skin
- 757.910 Unspecified anomalies of hair NOS
- 757.920 Unspecified anomalies of nail NOS
- 757.990 Unspecified anomalies of the integument NOS

- 758 Chromosomal Anomalies
- 758.0 Down syndrome
Clinical Down syndrome karyotype identified as:
- 758.000 Down syndrome, karyotype trisomy 21
 - 758.010 Down syndrome, karyotype trisomy G,NOS
 - 758.020 Translocation trisomy - duplication of a 21
 - 758.030 Translocation trisomy - duplication of a G, NOS
 - 758.040 mosaic Down
 - 758.090 Down syndrome NOS
- 758.1 Patau's syndrome
Clinical Patau's syndrome karyotype identified as:
- 758.100 Patau's syndrome, karyotype trisomy 13
 - 758.110 Patau's syndrome, karyotype trisomy D, NOS
 - 758.120 Translocation trisomy - duplication of a 13
 - 758.130 Translocation trisomy - duplication of a D, NOS
 - 758.190 Patau's syndrome NOS
- 758.2 Edwards's syndrome
Clinical Edwards's syndrome karyotype identified as:
- 758.200 Edwards syndrome, karyotype trisomy 18
 - 758.210 Edwards syndrome, karyotype trisomy E, NOS
 - 758.220 Translocation trisomy - duplication of an 18
 - 758.230 Translocation trisomy - duplication of an E, NOS
 - 758.290 Edwards's syndrome NOS
 - 758.295 Edwards's phenotype - normal karyotype

- 758.3 Autosomal deletion syndromes
- 758.300 Antimongolism syndrome
 Clinical antimongolism syndrome
 karyotype - partial or total deletion of:
 21
 G NOS
 NOS
- 758.310 Cri-du-chat syndrome
 Clinical Cri-du-chat syndrome
 karyotype - deletion of:
 5
 B NOS
 NOS
- 758.320 Wolff-Hirschorn syndrome
 Clinical Wolff-Hirschorn syndrome
 karyotype - deletion of:
 4
 B NOS
 NOS
- 758.330 Deletion of long arm of 13
 deletion of long arm of D NOS
- 758.340 Deletion of long arm of E
 deletion of long arm of 17 or 18
- 758.350 Deletion of short arm of E
 deletion of short arm of 17 or 18
- 758.360 Monosomy C mosaicism
- 758.380 Other loss of autosomal material
- 758.390 Unspecified autosomal deletion syndromes.
- 758.4 758.400 Balanced autosomal translocation in normal
 individual
- 758.5 Other conditions due to autosomal anomalies
- 758.500 Trisomy 8
- 758.510 Other trisomy C syndromes
 Trisomy: 6 10 11
 7 9 12
 C NOS
- 758.520 Other total trisomy syndromes
 Trisomy 22 Trisomy NOS
- 758.530 Partial trisomy syndromes
- 758.540 Other translocations
 Excludes:
 balanced translocation in normal individual
 (758.400)
- 758.550 Additional marker autosomes
- 758.580 Other specified anomalies of autosomes NOS
- 758.585 Polyploidy
- 758.586 Triploidy
- 758.590 Unspecified anomalies of autosomes

- 758.6 Gonadal Dysgenesis
 Excludes:
 pure gonadal dysgenesis (752.720)
 Noonan's Syndrome (759.800)
- 758.600 Turner's phenotype, karyotype 45, X [XO]
 758.610 Turner's phenotype, variant karyotypes
 karyotype characterized by:
 isochromosome mosaic, including XO
 partial X deletion
 ring chromosome
 Turner's phenotype, karyotype normal XX
 Use 759.800, Noonan's syndrome
- 758.690 Turner's syndrome, karyotype unspecified, NOS
 Bonneville-Ullrich syndrome NOS
- 758.7 Klinefelter's syndrome
- 758.700 Klinefelter's phenotype, karyotype 47, XXY
 758.710 Klinefelter's phenotype, other karyotype with
 additional X chromosomes
 XX
 XXXY
 XXYY
 XXXXY
- 758.790 Klinefelter's syndrome NOS
- 758.8 Other conditions due to sex chromosome anomalies
- 758.800 Mosaic XO/XY,45X/46XY
 Excludes: with Turner's phenotype (758.610)
- 758.810 Mosaic XO/XX
 Excludes: with Turner's phenotype (758.610)
- 758.820 Mosaic XY/XXY,46XY/47XXY
 Excludes: Klinefelter's phenotype (758.710)
- 758.830 Mosaic including XXXXY,49XXXXY
 Excludes: with Klinefelter's phenotype
 (758.710)
- 758.840 XYY, male, 47XYY
 Mosaic XYY male
- 758.850 XXX female,47XXX
- 758.860 Additional sex chromosomes NOS
- 758.880 Other specified sex chromosome anomaly
- 758.890 Unspecified sex chromosome anomaly
- 758.9 Conditions due to anomaly of unspecified chromosomes
- 758.900 Mosaicism NOS
- 758.910 Additional chromosome(s) NOS
- 758.920 Deletion of chromosome(s) NOS
- 758.930 Duplication of chromosome(s) NOS

- 759 Other and Unspecified Congenital Anomalies
- 759.0 Anomalies of spleen
- 759.000 Absence of spleen
 - Asplenia
 - 759.005 Ivemark's syndrome
 - 759.010 Hypoplasia of spleen
 - # 759.020 Hyperplasia of spleen
 - Splenomegaly
 - Hepatosplenomegaly (also use code 751.620)
 - 759.030 Misshapen spleen
 - 759.040 Accessory spleen
 - 759.050 Ectopic spleen
 - 759.080 Other specified anomalies of spleen
 - 759.090 Unspecified anomalies of spleen
- 759.1 Anomalies of adrenal gland
- 759.100 Absence of adrenal gland
 - 759.110 Hypoplasia of adrenal gland
 - 759.120 Accessory adrenal gland
 - 759.130 Ectopic adrenal gland
 - 759.180 Other specified anomaly of adrenal gland
 - Excludes:
 - congenital adrenal hyperplasia (use 255.200)
 - 759.190 Unspecified anomalies of adrenal gland
- 759.2 Anomalies of other endocrine glands
- 759.200 Anomalies of pituitary gland
 - 759.210 Anomalies of thyroid gland
 - 759.220 Thyroglossal duct anomalies
 - Thyroglossal cyst
 - 759.230 Anomalies of parathyroid gland
 - # 759.240 Anomalies of thymus
 - Thymic hypertrophy
 - 759.280 Other specified anomalies of endocrine gland
 - 759.290 Unspecified anomaly of endocrine gland

- 759.3 Situs inversus
 - 759.300 Dextrocardia with complete situs inversus
 - 759.310 Situs inversus with levocardia
 - 759.320 Situs inversus thoracis
 - 759.330 Situs inversus abdominis
 - 759.340 Kartagener's syndrome (triad)
 - 759.390 Unspecified situs inversus
 - Excludes: Dextrocardia (746.800) not associated with complete situs inversus

- 759.4 Conjoined twins
 - 759.400 Dicephalus
 - Two heads
 - 759.410 Craniopagus
 - Head joined twins
 - 759.420 Thoracopagus
 - Thorax-joined twins
 - 759.430 Xiphopagus
 - Xiphoid- and pelvis-joined twins
 - 759.440 Pygopagus
 - Buttock-joined twins
 - 759.480 Other specified conjoined twins
 - 759.490 Unspecified conjoined twins

- 759.5 759.500 Tuberosus sclerosis
 - Bourneville's disease
 - Epiloia

- 759.6 Other hamartoses, not elsewhere classified
 - 759.600 Peutz-Jegher's syndrome
 - 759.610 Encephalocutaneous angiomatosis
 - Kalischer's disease
 - Sturge-Weber syndrome
 - 759.620 Von Hippel-Lindau syndrome
 - 759.630 Gardner's syndrome
 - 759.680 Other specified hamartomas
 - 759.690 Unspecified hamartomas

- 759.7 # 759.700 Multiple congenital anomalies,
 - Anomaly, multiple NOS
 - Deformity, multiple NOS

759.8

Other specified anomalies and syndromes

- 759.800 Cong malformation syndromes affecting facial appearance
 - Cyclops
 - Noonan's Syndrome
 - Oral-facial-digital syndrome, type I
 - Oro-facial-digital syndrome, type II (Mohr's syndrome)
 - Waardenburg's syndrome
 - Whistling face syndrome
- 759.820 Cong malf. syndromes associated with short stature
 - Amsterdam dwarf (Cornelia de Lange syndrome)
 - Cockayne syndrome
 - Laurence-Moon-Biedl syndrome
 - Russell-Silver syndrome
 - Seckel syndrome
 - Smith-Lemli-Opitz syndrome
- 759.840 Congenital malformation syndromes involving limbs
 - Carpenter's syndrome
 - Holt-Oram syndrome
 - Klippel-Trenaunay-Weber syndromes
 - Rubenstein-Taybi syndrome
 - Sirenomelia
 - Thrombocytopenia Absent Radius (TAR) syndrome
- 759.860 Cong malformation syndromes with other skeletal changes
 - Marfan's syndrome
- 759.870 Cong malformation syndromes with metabolic disturbances
 - Alport's syndrome
 - Beckwith's (Wiedemann-Beckwith) syndrome
 - Leprechaunism
 - Meconium ileus
 - Menke's syndrome (kinky hair syndrome)
 - Prader-Willi syndrome
 - Zellweger's Syndrome
- 759.890 Other specified anomalies
 - Includes: Hemihypertrophy
 - Meckel-Gruber syndrome

759.9

Congenital anomaly, unspecified

- # 759.900 Anomalies of umbilicus
 - low-lying umbilicus
 - umbilical cord atrophy
- 759.910 Embryopathia NEC
- 759.990 Congenital anomaly NOS

214	Lipomas
214.0	214.000 Skin and subcutaneous tissue of face
	214.100 Other skin and subcutaneous tissue
	214.200 Intrathoracic organs
	214.300 Intra-abdominal organs
	214.400 Spermatic cord
	214.800 Other specified sites
	214.810 Lumbar or sacral lipoma paraspinal lipoma
	214.900 Lipoma, unspecified site

216 Benign Neoplasm of Skin

216.0 Benign neoplasm of skin
 Includes:
 blue nevus pigmented nevus
 papilloma dermatofibroma
 syringoadenoma * dermoid cyst
 hydrocystoma syringoma
 Excludes: skin of genital organs
 (221.0__-222.9__)

216.000 Skin of lip
 Excludes: vermillion border of lip (210.0)

216.100 Eyelid, including canthus
 Excludes: cartilage of eyelid (215.0)

216.200 Ear and external auditory canal
 Includes:
 auricle ear external meatus
 auricular canal external canal
 pinna
 Excludes: cartilage of ear (215.0)

216.300 Skin of other and unspecified parts of face
 Includes:
 cheek, external nose, external
 eyebrow temple

216.400 Scalp and skin of neck

216.500 Skin of trunk, except scrotum
 Includes:
 Axillary fold
 Perianal skin
 Skin of: chest wall
 abdominal wall
 groin
 buttock
 anus
 perineum
 back
 umbilicus
 breast
 Excludes:
 anal canal (211.4)
 anus NOS (211.4)
 skin of scrotum (222.4)

216.600 Includes: skin of upper limb, shoulder

216.700 Includes: skin of lower limb, hip

216.800 Other specified sites of skin
 Excludes: epibulbar dermoid cyst (use 743.810)

* 216.900 Skin, site unspecified
 Includes: hairy nevus
 sebaceous cyst

228.0 # Hemangioma
 Include: if greater than 4 inches diameter, if
 multiple hemangiomas, or if cavernous hemangioma

228.000 Of unspecified site
 # 228.010 Skin & subcutaneous -- unless otherwise specified
 228.020 Intracranial
 228.030 Retinal
 228.040 Intraabdominal
 228.090 Of other sites
 228.100 Cystic hygroma Lymphangioma, any site

771.0 Congenital infections (in utero infections only)

090.000 Congenital syphilis

771.000 Congenital rubella
 771.090 Unspecified TORCH infection

771.1 771.100 Cytomegalovirus (C.M.V.)

771.2 771.210 Toxoplasmosis

771.220 Herpes simplex
 Includes:
 encephalitis
 meningoencephalitis

771.280 Other specified congenital infection

774.4 774.480 Neonatal hepatitis, other specified
 774.490 Neonatal hepatitis, NOS

Other Specified Codes Used in Metro Atlanta Congenital Defects Program

List ordered alphabetically

524.000	Abnormalities of jaw size Micrognathia Macrogathia
255.200	Adrenogenital syndrome
270.200	Albinism
277.620	Alpha-1 antitrypsin deficiency
658.800	Amniotic bands (Constricting bands, amniotic cyst)
270.600	Arginosuccinic aciduria
778.000	Ascites, congenital
# 770.710	Bronchopulmonary dysplasia
453.000	Budd-Chiari, occlusion of hepatic vein
427.900	Cardiac arrhythmias, NEC
348.000	Cerebral cysts
330.100	Cerebral lipidoses (Includes: Tay Sachs disease, Gangliosidosis)
363.200	Chorioretinitis
277.000	Cystic Fibrosis No mention of meconium ileus
277.010	Cystic Fibrosis With mention of meconium ileus
279.110	DiGeorge syndrome
253.820	Diencephalic syndrome
# 767.600	Erb's palsy
425.300	Endocardial fibroelastosis
553.200	Epigastric hernia
# 368.000	Esotropia
# 378.000	Exotropia
# 351.000	Facial palsy
331.890	Familial degenerative CNS disease
760.710	Fetal alcohol syndrome
760.718	Probable Fetal alcohol syndrome (includes: 'facies')
760.750	Fetal hydantoin (dilantin) syndrome
282.200	G-6PD deficiency
271.000	Glycogen storage diseases
# 527.600	Gum cysts, Includes: mucocele
282.000	Hemolytic disease of the newborn
286.000	Hemophilia (all types)
774.480	Hepatitis - Other specified neonatal
202.300	Histiocytosis, malignant
# 769.000	Hyaline membrane disease
# 778.600	Hydrocoele, congenital
270.700	Hyperglycinemia
251.200	Hypoglycemia, idiopathic
252.100	Hypoparathyroidism, congenital
275.330	Hypophosphatemic rickets
253.280	Hypopituitarism, congenital
243.990	Hypothyroidism, congenital
345.600	Infantile spasms, congenital

550.000 Inguinal hernia
with mention of gangrene

550.900 Inguinal hernia no obstruction
with no mention of gangrene

550.100 Inguinal hernia with obstruction, (incarcerated)
with no mention of gangrene

560.000 Intussusception

208.000 Leukemia, congenital NOS

457.800 Lymphatics - Other specified disorders of

270.300 Maple syrup urine disease

777.000 Meconium ileus

777.600 Meconium peritonitis

777.100 Meconium plug

352.600 Moebius syndrome

520.600 Natal teeth

239.200 Neck cyst

159.800 Neoplasms of the abdomen, oth. spec.

191.000 Neoplasms of the CNS
Includes:
medulloblastoma
gliomas

171.800 Neoplasms of connective tissue
Includes:
Ewing's sarcoma
fibrosarcoma

155.000 Neoplasms of the liver
Includes:
hepatoblastoma
hemangio-epithelioma

162.800 Neoplasms of the lung

186.000 Neoplasms of the testes

194.000 Neuroblastoma

774.490 Neonatal hepatitis, NOS

774.480 Neonatal hepatitis, other specified

237.700 Neurofibromatosis

524.080 Pierre Robin syndrome

270.100 Phenylketonuria

685.100 Pilonidal sinus (sacrodermal), sacral sinus

277.630 Pseudocholinesterase enzyme deficiency

284.000 Red cell aplasia

362.600 Retinal degeneration, peripheral

190.500 Retinoblastoma

282.600 Sickle cell anemia

238.000 Teratoma, NOS

238.010 Teratoma, head and face

238.020 Teratoma, neck

238.030 Teratoma, abdomen

238.040 Teratoma, sacral, coccygeal

238.080 Teratoma, other specified

257.800 Testicular feminization syndrome

608.200 Torsion of the testes or spermatic cord

553.100 Umbilical hernia

286.400 von Willebrands disease

335.000 Werdnig Hoffman disease

189.000 Wilm's tumor (Nephroblastoma)

426.705 Wolfe-Parkinson-White syndrome, congenital

Other Specified Codes Used in Atlanta Surveillance System
List ordered by six digit code number

155.000 Neoplasms of the liver
Includes:
hepatoblastoma
hemangio-epithelioma

159.800 Neoplasms of the Abdomen, Oth. Spec.

162.800 Neoplasms of the Lung, Oth. Spec.

171.800 Neoplasms of Connective tissue
Includes:
Ewing's sarcoma
fibrosarcoma

186.000 Neoplasms of the testes

189.000 Wilm's tumor (nephroblastoma)

190.500 Retinoblastoma

191.000 Neoplasms of the CNS
Includes:
gliomas
medulloblastoma

194.000 Neuroblastoma

202.300 Histiocytosis, malignant

208.000 Leukemia, congenital NOS

238.000 Teratoma, NOS

238.010 Teratoma, head and face

238.020 Teratoma, neck

238.030 Teratoma, abdomen

238.040 Teratoma, sacral, coccyxgeal

238.080 Teratoma, other specified.

237.700 Neurofibromatosis

239.200 Neck cyst

243.990 Hypothyroidism, congenital

251.200 Hypoglycemia, idiopathic

252.100 Hypoparathyroidism, congenital

253.280 Hypopituitarism, congenital

253.820 Diencephalic syndrome

255.200 Adrenogenital syndrome (adrenal hyperplasia)

257.800 Testicular feminization syndrome

270.100 Phenylketonuria

270.200 Albinism

270.300 Maple syrup urine disease

270.600 Arginosuccinic aciduria

270.700 Hyperglycinemia

271.000 Glycogen storage diseases

275.330 Hypophosphatemic rickets

277.000 Cystic Fibrosis
No mention of meconium ileus

277.010 Cystic Fibrosis
With mention of meconium ileus

277.620 Alpha-1 antitrypsin deficiency

277.630 Pseudocholinesterase enzyme deficiency

279.110 DiGeorge syndrome

282.000 Hereditary spherocytosis

282.100 Hereditary elliptocytosis

282.600	Sickle cell anemia
282.300	G-6PD deficiency
284.000	Red cell aplasia
286.000	Hemophilia (all types)
286.400	von Willebrands disease
330.100	Cerebral lipidoses
	Includes:
	Tay Sachs disease
	Gangliosidosis
331.890	Familial degenerative CNS disease
335.000	Werdnig Hoffman disease
345.600	Infantile spasms; congenital
348.000	Cerebral cysts
# 351.000	Facial palsy
352.600	Moebius syndrome
362.600	Retinal degeneration, peripheral
363.200	Chorioretinitis
# 368.000	Esotropia
# 378.000	Exotropia
425.300	Endocardial fibroelastosis
426.705	Congenital Wolfe-Parkinson-White syndrome
427.900	Cardiac arrhythmias, NEC
453.000	Budd-Chiari, occlusion of hepatic vein
457.800	Other Specified Disorders of Lymphatics
# 520.600	Natal teeth
# 527.600	Gum cysts, Includes: mucocele
524.000	Abnormalities of jaw size
	Micrognathia
	Macrognathia
524.080	Pierre Robin syndrome
# 550.000	Inguinal hernia
	with mention of gangrene
# 550.100	Inguinal hernia with obstruction, (incarcerated)
	with no mention of gangrene
# 550.900	Inguinal hernia no obstruction
	with no mention of gangrene
# 553.100	Umbilical hernia
553.200	Epigastric hernia
# 560.000	Intussusception
# 608.200	Torsion of testes or spermatic cord
658.800	Amniotic bands (Constricting bands, amniotic cyst)
# 685.100	Pilonidal sinus (sacrodermal), sacral sinus
760.710	Fetal alcohol syndrome
760.718	Probable fetal alcohol syndrome (includes: 'facies')
760.750	Fetal hydantoin (dilantin) syndrome
# 767.600	Erb's palsy
# 769.000	Hyaline membrane disease
# 770.710	Bronchopulmonary dysplasia
# 777.100	Meconium plug
777.000	Meconium ileus
# 777.600	Meconium peritonitis
778.000	Ascites, congenital
# 778.600	Hydrocoele, congenital

PEDIATRIC EXAMINATION

In addition to record abstraction, a pediatric examination is proposed, following that developed for the original Boston Fetal Alcohol Syndrome (FAS) Study and recently revised for a new FAS study, based on the prior experience. This protocol is included here. The Project Director of the Planning Contract (Dr. McKinlay) collaborated in the development and reliability testing of this protocol.

Maternal Health Habits Study

BABY EXAM

Subject ID #	_____	1-01-:04
Instrument Type	<u> 1 </u> <u> 0 </u>	:05-:06
Card #	<u> 0 </u> <u> 1 </u>	:07-:08
Pregnancy # in Study	_____	:09-:10
Examiner	(1) DF _____ (2) SP _____ (3) JD _____ (4) BV _____ (5) _____ (6) _____ (7) _____	:11
Exam #	_____	:12
Date of Birth	_____ mo _____ day _____ year _____	:13-:18
Exam Date	_____ mo _____ day _____ year _____	:19-:24
Outcome of this pregnancy	_____	
(1) Liveborn		
(2) Stillborn		:25
(3) Post partum death		
I. INFANT PHYSICAL EXAM		
Was multiple contact necessary to complete exam?		
(1) Yes		:26
(2) No		
II. NEUROLOGICAL EXAM		
1.	Age in hours when neurological exam was done _____ (Round up over 1/2 hour)	:27-:29
2.	Minutes since last feed _____ (888 not fed (npo) 999 missing data)	:30-:32
3.	Adaptive Capacity - Perform only in predominant state 3 or less See code in Amiel, Tisson & Vitele	
a)	Respond to sound 0 1 2 9	:33
b)	Habituation to sound 0 1 2 9	:34
c)	Response to light 0 1 2 9	:35

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d)	Habituation to light	0	1	2	9	1:36
e)	Consolability	0	1	2	9	:37
	Specify from state 5 or state 6				—	:38
f)	Scarf sign	0	1	2	9	:39
g)	Recoil of elbows	0	1	2	9	:40
h)	Popliteal angle	0	1	2	9	:41
i)	Recoil of lower limbs	0	1	2	9	:42
j)	Active contraction of neck flexors	0	1	2	9	:43
k)	Active contraction of neck extensors	0	1	2	9	:44
l)	Palmar grasp	0	1	2	9	:45
m)	Response to traction	0	1	2	9	:46
n)	Supporting reaction	0	1	2	9	:47
o)	Automatic walking	0	1	2	9	:48
p)	Moro reflex	0	1	2	9	:49
q)	Sucking	0	1	2	9	:50
r)	Alertness	0	1	2	9	:51

Crying

(0)	Absent	
(1)	Weak	
(2)	Normal	:52
(3)	Excessive	
(9)	Not done	

Motor Activity

(0)	Absent	
(1)	Diminished	
(2)	Normal	:53
(3)	Mildly excessive	
(4)	Grossly excessive	
(9)	Not done	

Tremulousness

- (0) Not done
- (1) No tremors or tremulousness noted
- (2) Tremors only during sleep
- (3) Tremors only after the Moro or startles
- (4) Tremulousness seen 1 or 2 times in states 5 or 6 1:54
- (5) Tremulousness seen 3 or more times in states 5 or 6
- (6) Tremulousness seen 1 or 2 times in state 4
- (7) Tremulousness seen 3 or more times in state 4
- (8) Tremulousness seen in several states
- (9) Tremulousness seen consistently in all states

Tremor Frequency

- (1) < 6 times per seconds
- (2) > 6 times per second :55
- (3) Not applicable, no tremor
- (9) Not recorded

Tremor Amplitude

- (1) < 3 cm
- (2) > 3 cm :56
- (3) Not applicable, no tremor
- (9) Not recorded

4. Predominant states (2) during neurological exam

Most predominant state _____ :57

Next most predominant state _____ :58

III. ANTHROPOMETRIC

Specify age in hours _____ :59-:61

- 1. Length _____ cm. :62 - :64
- 2. Head _____ cm. :65-:67
- 3. Right palpebral fissure _____ cm. :68-:69
- 4. Intercanthal distance _____ cm. :70-:71
- 5. R ear length _____ cm. :72-:73
- 6. L ear length _____ cm. :74-:75

7.	R subscapular skinfold	___ . ___	mm.	1:76-:78
	ID#	___		2:01-04
	Type	<u>1</u> <u>0</u>		:05-:06
	Card #	<u>0</u> <u>2</u>		:07-:08
	Pregnancy #	___		:09-:10
8.	L subscapular skinfold	___ . ___	mm.	:11-:13
9.	R arm circumference	___ . ___	cm.	:14-:16
10.	L arm circumference	___ . ___	cm.	:17-:19
11.	Right triceps	___ . ___	mm.	:20-:22
12.	Left triceps	___ . ___	mm.	:23-:25
13.	Penile length	___ . ___	cm.	:26-:27

IV. GENERAL AND DYSMORPHIC EXAM

1. Sex
 - (1) Male
 - (2) Female
 - (3) Ambiguous:28

2. Anomalies

Code as follows:

- | | |
|------------------------|----------------------------------|
| (0) Absent | (3) Present Multiple (3 or more) |
| (1) Present Unilateral | (9) Exam could not be done |
| (2) Present Bilateral | |

Head-Major

a)	Hydrocephaly	0	1	2	3	9	:29
b)	Anencephaly	0	1	2	3	9	:30
c)	Encephalocele	0	1	2	3	9	:31
d)	Craniosostenosis	0	1	2	3	9	:32
e)	Other	0	1	2	3	9	:33

Head-Minor

a)	Metopic fontanel or suture open to glabella	0	1	2	3	9	:34
----	---	---	---	---	---	---	-----

b) Scalp Defect	0	1	2	3	9	:2:35
c) Absent whorl	0	1	2	3	9	:36
d) 2 or more hair whorls	0	1	2	3	9	:37
e) Frontal Hair upswEEP	0	1	2	3	9	:38
f) Other _____	0	1	2	3	9	:39

Ears-Major

a) non patent canal	0	1	2	3	9	:40
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Ears-Minor

a) Preauricular skin tag	0	1	2	3	9	:41
b) Preauricular sinus or pit	0	1	2	3	9	:42
c) Malformed ears	0	1	2	3	9	:43
d) Posteriorly rotated ears (more than 15°)	0	1	2	3	9	:44

Eyes

a) Lid Coloboma	0	1	2	3	9	:45
b) Iris Coloboma	0	1	2	3	9	:46
c) Brushfield spots	0	1	2	3	9	:47
d) Epicanthal folds	0	1	2	3	9	:48
e) Synophrys	0	1	2	3	9	:49
f) Upslanting palpebral fissures	0	1	2	3	9	:50
g) Downslanting palpebral fissures	0	1	2	3	9:	:51
h) Ptosis	0	1	2	3	9	:52
i) Other: Specify _____	0	1	2	3	9	:53

Nose-Major

a) Choanal atresia 0 1 2 3 9 2:54

Nose-Minor

a) Smooth or indistinct philtrum 0 1 2 3 9 :55

b) Flat nasal bridge 0 1 2 3 9 :56

c) Anteverted nares 0 1 2 3 9 :57

Oropharynx

a) Cleft lip 0 1 2 3 9 :58

b) Cleft palate 0 1 2 3 9 :59

c) Thin upper lip 0 1 2 3 9 :60

d) Short mandible 0 1 2 3 9 :61

e) Broad alveolar ridge 0 1 2 3 9 :62

f) Other: Specify _____ 0 1 2 3 9 :63

Neck

a) Cyst 0 1 2 3 9 :64

b) Goiter 0 1 2 3 9 :65

c) Branchial sinus 0 1 2 3 9 :66

d) Webbed 0 1 2 3 9 :67

e) Other: _____ 0 1 2 3 9 :68

Chest

a) Pectus excavatum 0 1 2 3 9 :69

b) Accessory nipples 0 1 2 3 9 :70

c) Areolar skin tag 0 1 2 3 9 :71

d) Other: _____ 0 1 2 3 9 :72

Abdomen

a)	Gastroschisis	0	1	2	3	9	2:73
b)	Omphalocele	0	1	2	3	9	:74
c)	Diaphragmatic hernia	0	1	2	3	9	:75
d)	Single umbilical artery	0	1	2	3	9	:76
e)	Liver more than 3 cm (below RCM)	0	1	2	3	9	:77
f)	Kidney more than 3 cm wide to palpation	0	1	2	3	9	:78
g)	Abdominal mass	0	1	2	3	9	:79
h)	Other:	0	1	2	3	9	:80

ID# _____
 Type 1 0 _____
 Card # 0 3
 Pregnancy # _____

3:01-04
 :05-:06
 :07-:08
 :09-:10

Extremities

a)	Phocomelia	0	1	2	3	9	:11
b)	Polydactyly hands	0	1	2	3	9	:12
c)	Polydactyly feet	0	1	2	3	9	:13
d)	Clinodactyly (more than 8° 5th finger)	0	1	2	3	9	:14
e)	Camptodactyly	0	1	2	3	9	:15
f)	Hypoplastic fingernail	0	1	2	3	9	:16
g)	Simian or bridged simian crease	0	1	2	3	9	:17
h)	More than 1/4 inch between 1st & 2nd toe	0	1	2	3	9	:18
i)	Syndactyly more than 1 tp 2nd & 3rd toes	0	1	2	3	9	:19

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j)	Calcaneovalgus	0	1	2	3	9	3:20
k)	Clubbed foot talipes equinovarus	0	1	2	3	9	:21
l)	Dislocated hip: Con- firmed by x-ray assess- ment in first 14 days	0	1	2	3	9	:22
m)	Inability to supinate forearm	0	1	2	3	9	:23
n)	Other joint limitations-Specify:	0	1	2	3	9	:24
o)	Other: _____	0	1	2	3	9	:25

Back

a)	Meningo myelocele	0	1	2	3	9	:26
b)	Vertebral anomalies	0	1	2	3	9	:27
c)	Scoliosis	0	1	2	3	9	:28
d)	Sacral hypoplasia	0	1	2	3	9	:29
e)	Pilonoidal sinus	0	1	2	3	9	:30
f)	Deep presacral dimple	0	1	2	3	9	:31
g)	Other: _____	0	1	2	3	9	:32

Skin

a)	Hemangiomas (other than stork bites)	0	1	2	3	9	:33
b)	Pigmented Nevi	0	1	2	3	9	:34
c)	Mongolian spots other than buttocks	0	1	2	3	9	:35
d)	Cafe au lait spots	0	1	2	3	9	:36
e)	Other: _____	0	1	2	3	9	:37

Genitalia

a) Inguinal hernia 0 1 2 3 9 3:38

Female

a) Clitoral hypertrophy 0 1 2 3 9 :39

b) Vaginal skin tag 0 1 2 3 9 :40

c) Labial hypoplasia 0 1 2 3 9 :41

d) Other: _____ 0 1 2 3 9 :42

Male

a) Hypospadias 0 1 2 3 9 :43

If yes, specify:

1st degree

2nd degree

3rd degree

_____ :44

b) Chordee 0 1 2 3 9 :45

c) Cryptorchidism 0 1 2 3 9 :46

d) Other: _____ 0 1 2 3 9 :47

V. NEONATAL RECORD REVIEW

1. Ordinal Position of this birth

(0) Singleton

(1) Twin A

(2) Twin B

(3) Triplet C

(4) Other _____

:48

2. Gestational Age by Dubowitz: _____ weeks :49-:51

(1) Study Pediatrician

(2) Other Pediatrician

(3) Not done (gestational age by LMP)

:52

3. Birth weight _____ grams :53-:56

4. Apgar 1 _____ :57-:58

5. Apgar 5 _____ :59-:60

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6. Number Days in Special Care ____ ____ ____ (code 1 for up to 24 hours) 3:61-:63
7. Number Days Post-partum hospitalization ____ ____ ____ :64-:66
8. Information from record review only
- (1) Yes :67
(2) No
9. If yes, specify reason
- (1) Baby transferred due to illness :68
(2) Baby discharged before examined
(3) NA - Baby examined
10. Condition at discharge from nursery
- (1) Alive-discharged to home or foster home :69
(2) Dead
(3) Transferred to another hospital or another ward at BCH
11. If dead, age at death ____ ____ ____ days (code 001 for up to 24 hours) :70-:72
(code 000 for alive)
12. Medications:
- (00) None (except Vit K and eye prophylaxis)
(01) Chlorpromazine
(02) Barbiturates
(03) Dilantin
(04) Theophyllin/Caffeine :73-:74
(05) Antibiotics
(06) Diuretics
(07) Digitalis preparation
(08) Other _____
(09) Missing data
(10) Multiple meds (from list above)(circle all relevant above)
13. Maximum Bilirubin in chart ____ ____ :75-:77
14. Age in hours. Maximum bili recorded ____ ____ ____ (hours) :78-:80
- ID# _____ 4:01-:04
Type 1 0 _____ :05-:06
Card # 0 4 _____ :07-:08
Pregnancy # _____ :09-:10

VI. GENERAL

	<u>Noted</u>	<u>Not Noted</u>	
1. Intubate for visualization	(1)	(2)	4:11
2. Intubate for meconium	(1)	(2)	:12
3. Intubate for resuscitation	(1)	(2)	:13
4. Bagged at birth	(1)	(2)	:14
5. Feeding problem requiring gavage	(1)	(2)	:15

VII. RESPIRATORY

1. RDS	(1)	(2)	:16
2. Meconium aspiration syndrome	(1)	(2)	:17
3. Congenital pneumonia	(1)	(2)	:18
4. Apnea	(1)	(2)	:19
5. Other respiratory distress	(1)	(2)	:20
6. Transient tachypnea	(1)	(2)	:21
7. PFC	(1)	(2)	:22
8. BPD	(1)	(2)	:23
9. Pneumothorax	(1)	(2)	:24

VIII. METABOLIC DISORDERS

1. Hypoglycemia <40	(1)	(2)	:25
2. Hypocalcemia <7.5	(1)	(2)	:26
3. Hypothyroidism	(1)	(2)	:27
4. Jitteriness or hyperactivity without specific causes	(1)	(2)	:28

IX. CARDIAC

1. Major cardiac anomalies which require immediate catheterization within 14 day of birth Specify _____	(1)	(2)	4:29
2. Congestive Heart Failure	(1)	(2)	:30
3. Cardiac anomalies not requiring immediate catheterization within 14 days of birth Specify _____	(1)	(2)	:31
4. Persistent cyanosis (cardiac)	(1)	(2)	:32
5. Murmur	(1)	(2)	:33

X. HEMATOLOGIC PROBLEMS

1. Phototherapy	(1)	(2)	:34
2. Exchange transfusion for bili	(1)	(2)	:35
3. Reduction transfusion	(1)	(2)	:36
4. Hemorrhagic diathesis	(1)	(2)	:37
5. Anemia noted within 72 hours	(1)	(2)	:38
6. Polycythemia noted within 72 hours	(1)	(2)	:39

XI. SEPSIS

1. v/o sepsis workup	(1)	(2)	:40
2. sepsis diagnosed	(1)	(2)	:41

XII. CNS

1. CNS depression > 24 hours	(1)	(2)	:42
2. CNS depression < 24 hours	(1)	(2)	:43
3. Withdrawal syndrome	(1)	(2)	:44
4. Seizures	(1)	(2)	:45
5. Non-chromosomal syndrome Specify.	(1)	(2)	:46

6. Chromosomal syndrome (1) (2) 4:47
Specify _____

XIII. GI

1. Necrotizing enterocolitis suspected (1) (2) :48

2. Necrotizing enterocolitis confirmed (1) (2) :49

3. Other GI problems (1) (2) :50
Specify _____

XIV. RENAL

1. ATN (1) (2) :51

2. Hydronephrosis (1) (2) :52

3. Other (specify) (1) (2) :53

XV. CONGENITAL INFECTIONS

1. Syphilis (1) (2) :54

2. Herpes (1) (2) :55

3. CMV (1) (2) :56

4. Toxo (1) (2) :57

5. Other (specify) (1) (2) :58

XVI. NEONATAL SURGERY

1. Circumcision (1) (2) :59

2. Other (specify) _____ (1) (2) :60

Specify if palpebral fissure :61

1) Open spontaneously

2) Pried open

9) Not done

Raw Score of Dubowitz :62

Neurologic _____ :63-64

Physical _____ :65-66

STUDY DESIGN PROTOCOL

APPENDICES

DELIVERABLE D

1. INFORMED CONSENT AND RELEASE FORMS
2. CONGENITAL ABNORMALITY CLASSIFICATION AND PEDIATRIC EXAMINATION
3. MYOCARDIAL INFARCTION, SUDDEN DEATH AND STROKE CLASSIFICATION
4. NEUROBEHAVIORAL TESTING PROTOCOL
5. SOFT TISSUE SARCOMA CLASSIFICATION
6. PROTOCOL FOR 2, 3, 7, 8 - TCDD BODY BURDEN DETERMINATION

MYOCARDIAL INFARCTION.

SUDDEN DEATH

AND STROKE

CLASSIFICATION

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While it is well recognized that coronary heart disease mortality has declined in the United States during the past two decades, the reasons remain obscure. A major factor in our inability to fully understand the process has been a lack of information on disease morbidity rates, through which better understanding of mortality trends might occur. Three major research projects are currently in place in the United States that should provide insights into the cause of coronary heart disease mortality changes. These three programs testing community based cardiovascular disease prevention strategies are the Stanford Five-City Program, the Minnesota Heart Health Program, and the Pawtucket Heart Health Program. All are conducting ongoing surveillance for in-hospital myocardial infarcts and coronary heart disease mortality in a combined total of 13 communities totaling over 850,000 people. Two other major initiatives include similar surveillance activities. The Atherosclerosis Risk In Communities Study of the National Heart, Lung and Blood Institute has evolved from the Community Cardiovascular Surveillance Pilot Study and includes surveillance in four communities across the United States. Although the populations under morbidity and mortality surveillance are smaller in the Atherosclerosis Risk in Communities Study than in the three community studies, a larger number of known or potential risk factor variables will be studied and related to disease outcomes. The multi-national monitoring program for cardiovascular disease outcomes sponsored by the World Health Organization (MONICA) is a cooperative study using similar protocols across many countries seeking to understand differential morbidity and mortality rates on a nation-to-nation basis.

Each of these, and other similar research initiatives requires accurate, easily applied, and cost-efficient methods for surveillance of cardiovascular disease endpoints. Developmental work has been ongoing in the design of such methods in the United States and elsewhere and has resulted in steadily

improving criteria and algorithms for coronary heart disease surveillance. Criteria and algorithms which originated in the Minnesota Heart Survey and have been utilized in the early stages of the three community projects have been published (1). Similar methods currently are being applied by MONICA, were utilized by the Community Cardiovascular Surveillance Pilot and will be employed in the recently funded Atherosclerosis Risk in Communities Study.

In order to facilitate collaboration among the three community projects at Stanford, Minneapolis and Pawtucket, the National Heart, Lung and Blood Institute provided additional, separate funding in July, 1981 to form a Coordinating Committee for Community Demonstrations Studies (CCDS). The major goal of this coordinating effort has been, wherever possible, to develop common outcome measurements for risk factors and for morbid and mortal events. Comparability of these outcome estimates, in turn, may enhance the interpretability and impact of conclusions from these community-based cardiovascular disease prevention research programs. The Evaluation Subcommittee of the Coordinating Committee of Community Demonstration Studies, consisting of the authors of the present paper, has carried out substantial developmental and pilot work on the surveillance approach for detecting cases of hospitalized acute myocardial infarction.

The present trilogy of papers reports this pilot work, focusing upon applications of different diagnostic algorithms. The goal has been to produce a robust algorithm of high sensitivity and specificity, applicable in all three projects, for in-hospital nonfatal myocardial infarction (including in-hospital fatalities after diagnosis). Attributes of importance include robustness in the face of potential shifts in diagnostic categorization as may occur, for example, in the recently instituted Diagnosis Related Group hospital reimbursement policies. The approach should also be applicable across a wide range of medical

record content and be stable in the face of evolving diagnostic testing procedures.

In the present series of papers, the algorithm originally developed by Gillum and colleagues (1) has been used as the Reference Algorithm (presented diagrammatically in Figure 1). Conceptually, this Reference Algorithm does not give differential weight to the hospital discharge diagnoses (as indicated by ICD-9 code) of cases screened. The diagnostic codes used most widely are ICD-9 410-414, although other codes can also be screened.

Three diagnostic components are abstracted from the medical record of screened cases. Cardiac enzymes including creatine kinase (CK), lactic dehydrogenase, and aspartate amino transferase are directly copied from the record along with laboratory-specific information on the upper limits of normal in order to categorize enzyme levels. Any electrocardiograms are copied and subsequently coded according to the Minnesota code. The third component abstracted from the medical record is presence or absence, and (if present) duration and character of chest pain. Substantial abstractor judgement is required to determine the length, location, and quality of the pain. Moreover, many medical records unfortunately contain no or very incomplete information on this item.

As shown in Figure 1, the first priority for diagnosis is placed on the electrocardiogram (ECG) in the Reference Algorithm. An evolving diagnostic ECG suffices to conclude that an acute myocardial infarction occurred. A diagnostic electrocardiogram with abnormal enzymes also results in a diagnosis of definite myocardial infarction. In the absence of a diagnostic electrocardiogram, only the combination of prolonged pain and abnormal enzymes results in a conclusion of definite myocardial infarction.

The time and abstractor judgement required to abstract medical records for the Reference Algorithm, combined with the frequently inadequate medical record documentation of pain, led the Coordinating Committee Evaluation Subcommittee to investigate other potential algorithms with enhanced repeatability and equivalent validity. The algorithm presented in Figure 2 was developed to meet these goals. Several features represent conceptual changes from the Reference Algorithm. The first is the departure from the usual anterospective clinical process in which the character of pain and the electrocardiogram are critical diagnostic components. In the new CCCDS Algorithm, the role of pain and of the electrocardiogram have been subjugated to that of creatine kinase. Duration and quality of chest pain is not considered. Further, cases which have already been judged clinically to represent acute coronary heart disease events (ICD-9 CM codes 410 & 411) are treated differently from cases which have not (codes 412-414 and any additional screening codes). For example, the absence of a mention of chest pain in the record has been equated with presence of pain for cases with diagnostic codes 410 and 411 rather than with the absence of pain, as in the Reference Algorithm.

In essence, the resulting algorithm treats abnormal creatine kinase as diagnostic of acute myocardial infarction if it occurs in the presence of a hospital discharge diagnosis coded as ICD 9 CM 410 or 411. In the presence of equivocal enzymes, an evolving or diagnostic electrocardiogram also yields a definite myocardial infarction diagnosis in cases coded 410 or 411. Cases with codes other than 410-411 can reach a definite infarct diagnosis only if enzymes are abnormal and the electrocardiogram is evolving or diagnostic and pain is present. If enzymes are normal or equivocal for these cases, the only diagnoses possible under the CCCDS Algorithm are possible myocardial infarction or non-event.

The accompanying papers address a number of issues comparing the Reference and the CCCDS Algorithms. The CCCDS Algorithm, by minimizing abstractor judgement and decisions by medical review panels, is designed to be compatible with direct data entry and with computerized application of the criteria for diagnostic categorization. The cost and reproducibility of the abstracting process are considered in the paper by McKinlay and colleagues. Differential sensitivity and specificity of variations on the CCCDS Algorithm are discussed in detail by Mascioli and colleagues. The paper by Fortmann directly compares diagnoses derived from application of the Reference Algorithm, as used in the Stanford Study, to those using the CCCDS Algorithm.

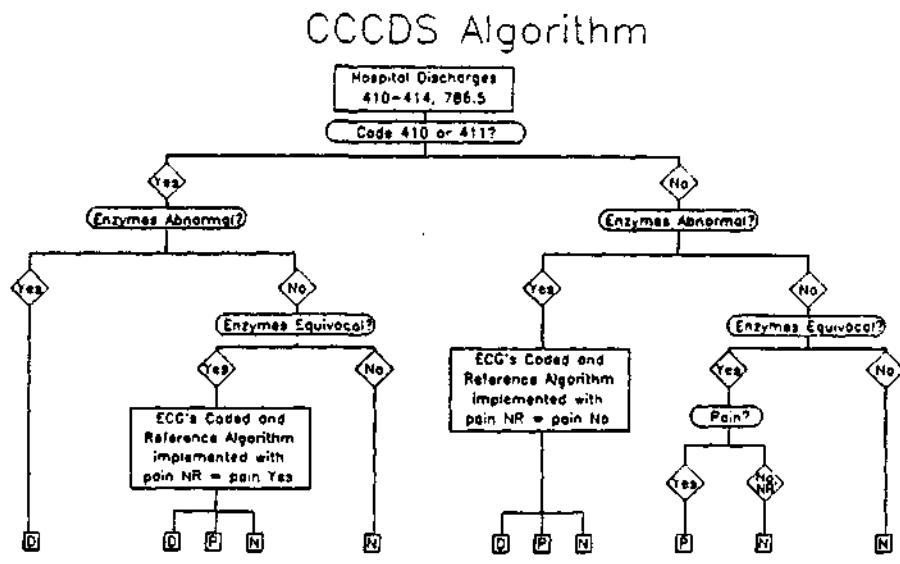
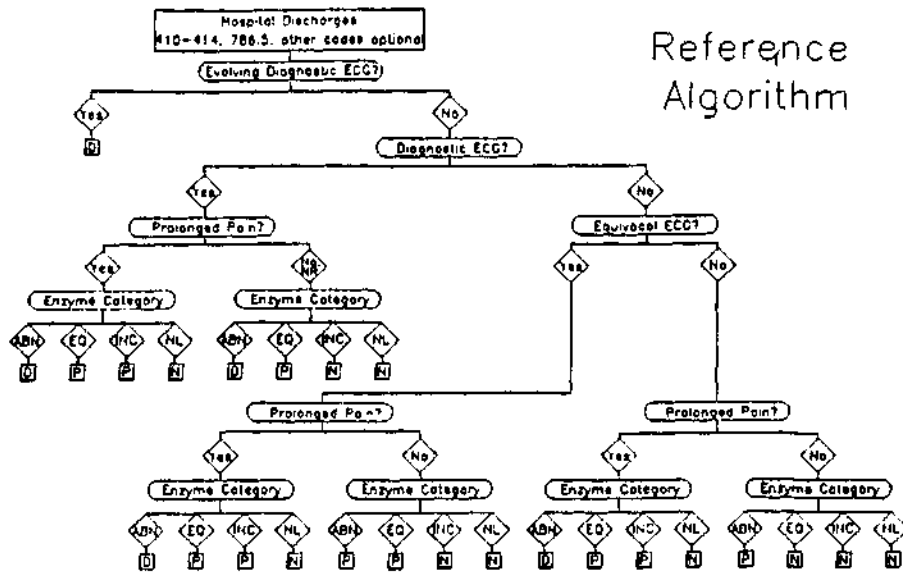
The results presented by these papers indicate that the CCCDS Algorithm represents a potentially important advance in heart disease surveillance methodology.

LEGENDS

- Figure 1: Reference Algorithm for myocardial infarction surveillance derived from work of Gillum and colleagues. Abnormal enzymes = at least twice normal. Equivocal enzymes = above normal, but not twice normal. D = definite and P = possible myocardial infarction. N = no event.
- Figure 2: Revised CCCDS Algorithm for myocardial infarction surveillance. For criteria and abbreviations, see Figure 1.

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International diagnostic criteria for acute myocardial infarction and acute stroke

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Almost every investigator studying the occurrence, causes, treatment, or prevention of myocardial infarction or stroke will at some time require an explicit set of diagnostic criteria to classify potential cases on the basis of retrospectively collected data.¹ These data may come from hospital records, clinic records, autopsy or coroner's reports, next-of-kin interviews, and death certificates. Direct patient interview or examination often will be impractical or impossible, and baseline ECGs and neurologic examinations unavailable.

The desire to study the determinants of the recent sharp downward trends in ischemic heart disease and stroke death rates as well as the need to evaluate morbid outcomes in community trials or cardiovascular disease prevention have led to the widespread application of community surveillance of hospitalizations for cardiovascular morbidity. This methodology, its problems, and applications have been reviewed recently.² In the past, each study developed its own diagnostic criteria, making interstudy comparisons difficult. The current interest in explaining national mortality trends by examining morbidity and case fatality rates in many centers around the world calls for a concerted effort toward interstudy standardization of methods. This would enable the application of a single set of criteria to data collected in all centers, even though centers may wish to use other criteria for specific purposes. Diagnostic criteria developed for use in longitudinal

prospective studies or in clinical trials probably will not be suitable when information for the diagnostic classification of potential cases must be abstracted from hospital records. The baseline data readily available in prospective cohort studies or clinical trials frequently are missing, equivocal, or uninterpretable in clinical records. Therefore, criteria must be formulated with particular regard to these limitations and must allow for cardiovascular events to be classified as definite or possible according to the degree of specificity of the criteria which have been met. The combined class of definite and possible cases should be highly sensitive to the event under study at the cost of lowered specificity, whereas the group of definite cases should be sufficiently specific to be used in etiologic research, where it is preferable to erroneously exclude some true cases than to include noncases. Excluding true cases reduces sample size and perhaps generalizability of findings, while including noncases dilutes by misclassification any associations that may be present within the study sample.

The need for explicit, high-quality diagnostic criteria has become more generally recognized since an earlier report in 1964.³ At that time many published studies stated no criteria, and many of those stated were highly subjective in nature. In response to the need for a uniform set of procedures and criteria for interstudy comparisons of morbidity rates, we undertook to refine a set of diagnostic criteria previously used for community surveillance of myocardial infarction and stroke.^{4,7} All or parts of the set of criteria developed are currently being used with major or minor modifications by the Minnesota Heart Survey (MHS),^{8,9} the Minnesota Heart Health Program, the Stanford Five City Project, the Pawtucket Heart Health Program, and three large community intervention demonstration programs. These criteria were major inputs to the criteria independently developed by the Multicenter Community Cardiovascular Surveillance Program (CCSP)

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Table I. Characteristics of criteria used in community surveillance population studies of myocardial infarction

Characteristics	n
Total number of studies in each group	24
Written criteria published	18
Source of criteria	
Self-designed	14
WHO	6
No explicit criteria	4
Explicit criteria given for	
ECG	11
Enzymes	9
Clinical judgment use	
Unknown	
1+	1
2+	5
3+	8
4+	6
Evaluation published of	
Validity	0
Repeatability	1

Table II. Characteristics of criteria used in community surveillance population studies of stroke

Characteristics	n
Total number of studies	16
Written criteria published	9
Source of criteria	
Self-designed	5
WHO	2
NINDB 1958	2
No explicit criteria	6
Other	1
Explicit criteria given	
Neurologic symptoms and signs	3
CT scan	1
Other laboratory findings	5
Clinical judgment use	
1+	1
2+	0
3+	4
4+	4
Unknown	7
Evaluation published of	
Validity	0
Repeatability	0

of the National Heart, Lung and Blood Institute and the World Health Organization (WHO)-coordinated Project on Multinational Monitoring of Trends and Determinants in Cardiovascular Diseases (MONICA). Extensive testing of the validity, repeatability, and sensitivity of these criteria is currently being conducted.⁹ Computer algorithms have been written and tested for application in the MHS. This report seeks to review previously used criteria and to make the currently recommended criteria and the instructions for their use available to all investigators planning studies of acute myocardial infarction, ischemic heart disease death, and stroke so that their results may be more directly comparable to those of other current studies.

PREVIOUS CRITERIA

A previous report analyzed criteria used in 57 studies of myocardial infarction published prior to 1964.³ A review of the criteria used in all subsequent published studies of myocardial infarction and stroke is beyond the scope of this article. However, a selective review was performed of several types of studies.

The criteria of the Framingham Heart Study,¹⁰ a community-based cohort study, were reviewed. This study developed its own criteria for myocardial infarction, which included fairly explicit criteria for interpreting the ECG and serum glutamic oxaloacetic transaminase (SGOT) levels obtained from review of hospital records from the suspected acute event. However, the degree of explicitness of criteria

was sufficiently low to require considerable use of subjective clinical judgment by the diagnostic review panel. Reports on the validity or repeatability of diagnoses derived from the process have not been published. Stroke criteria were also self-designed but tended to be less explicit, with heavy reliance on the clinical judgment of the review panel.

The criteria of the only published nationwide cross-sectional survey, the Health Examination Survey, 1960-62,¹³ were reviewed. Detailed written criteria for myocardial infarction, derived from New York Heart Association criteria, were published. They included explicit criteria for chest pain history and ECG, and required relatively little use of clinical judgment in their application. A repeatability study of diagnostic assignment was published.

Characteristics of diagnostic criteria used by 24 published community surveillance studies of myocardial infarction and stroke are shown in Tables I and II. Other features of these studies have been previously summarized.² Hospital records were used by all as the primary data source, often supplemented by autopsy records and office records. The criteria of the WHO were used by several European studies including the WHO myocardial infarction and stroke registers.¹⁴ WHO criteria as revised in 1971 included explicit ECG criteria but required great use of clinical judgment for diagnosis of myo-

cardial infarction. WHO stroke criteria were not explicit, relying almost entirely on clinical judgment. One study of repeatability was done in North Karelia, Finland.¹⁵ The prospective Health Insurance Plan of New York study¹⁶ and the retrospective Kaiser-Permanente study¹⁷ have both published self-designed criteria for myocardial infarction, which are explicit for ECG and enzymes.

A series of major clinical trials of the secondary or primary prevention of ischemic heart disease death, myocardial infarction, and/or stroke have each developed diagnostic criteria for their end points. However, only a few have published their criteria. The Coronary Drug Project designed criteria for recurrent myocardial infarction, which were explicit for ECGs but not for enzymes or clinical symptoms.¹⁸ There was heavy reliance on clinical judgment in assigning the diagnosis. Stroke criteria were reasonably explicit regarding neurologic symptoms and signs but still relied heavily on clinical judgment. The Aspirin Myocardial Infarction Study also developed criteria for recurrent infarction, which included explicit ECG and enzyme criteria.¹⁹ Stroke criteria were less explicit. Little clinical judgment was required to diagnose myocardial infarction but much more to diagnose stroke.

Studies varied considerably in the content and application of criteria. Those adopting WHO criteria usually modified them before use. In the few studies publishing explicit ECG criteria, the only common ground was that a new pathologic Q wave was diagnostic of definite myocardial infarction. Other studies accepted various combinations of Q waves, ST and T wave changes, and clinical symptoms as also diagnostic of definite infarction. Although the Minnesota code¹ was sometimes used in criteria to describe ECG changes, it was seldom formally applied except in United States multicenter clinical trials.^{18,19} Likewise, the few studies publishing explicit enzyme criteria showed great variation in the requirements for the diagnosis of definite infarction. The one area of agreement was that enzyme elevations alone were not sufficient.

DEVELOPMENT AND EVALUATION OF CRITERIA

The following are specific goals pursued in the development of a refined set of criteria: (1) Create a set of validated cardiovascular disease event criteria, which maximize reliability by minimizing the need for "clinical judgment." (2) Minimize the need for manual calculations and manual algorithm application. (3) Minimize the use of implicit assumptions, criteria, or values. (4) Maximize the use of data usually found on a hospital chart, while avoiding a level of stringency that precludes applications to

records that were collected without research in mind.

The criteria should also maintain validity by allowing "clinical judgment" to override the algorithm when it is apparent that the algorithm cannot deal with a specific case. The criteria should be based on symptoms, physical signs, tests, and other data validated or accepted as valid by the practicing medical community. This implies the following course of events: (1) Make a first draft of criteria based on "best judgment" and a literature review. (2) Make a first draft of chart abstracting forms based on the criteria. (3) Test whether data required for application of criteria are available, whether the forms can deal with the situations arising in hospital records, and whether the forms present the data to accurately reflect the sense of the record. (4) Continue to correct and update the criteria and forms in a feedback loop until steps 2 and 3 above are satisfactorily met. (5) Test reliability at the following levels: (a) Are multiple abstractors able to abstract the chart reaching the same conclusion in a sufficient proportion of cases? (b) Can the criteria be correctly applied to the abstracts in a satisfactory proportion of the cases? (c) If computer programs are used: Do they accurately reflect the logic of the criteria? Can they be applied with minimal data editing? Are they free of logic flaws or other "bugs"? Do they identify situations in which the algorithm is likely to reach an inappropriate conclusion? (d) After errors are eliminated, does reliability of diagnosis meet *a priori* defined criteria? (6) Test validity by the following methods: (a) Present the conclusions of criteria to a panel of experts. (b) Apply criteria to a set of cases with unusually complete data and compare conclusions reached with the "full" and the "reduced" data set. (For example, to test the robustness of the criteria when enzymes alone are present on a record, apply the criteria to the complete data set and then to the data set with all the information except enzyme values deleted.) The criteria are valid to the extent that the conclusions from the "reduced" data set correspond to the conclusions from the complete data set. (c) Apply the criteria to a set of autopsied cases including and excluding autopsy information. (Good agreement with and without autopsy data would support the validity of the criteria in nonautopsied cases).

The initial set of criteria proposed here was built upon those of the Framingham Cardiovascular Disease Survey,^{4,7} which were designed in the early 1970s drawing heavily upon the criteria used in the Framingham Heart Study.¹⁰ The criteria of all the recent major cardiovascular clinical trials in the United States were reviewed with the assistance of

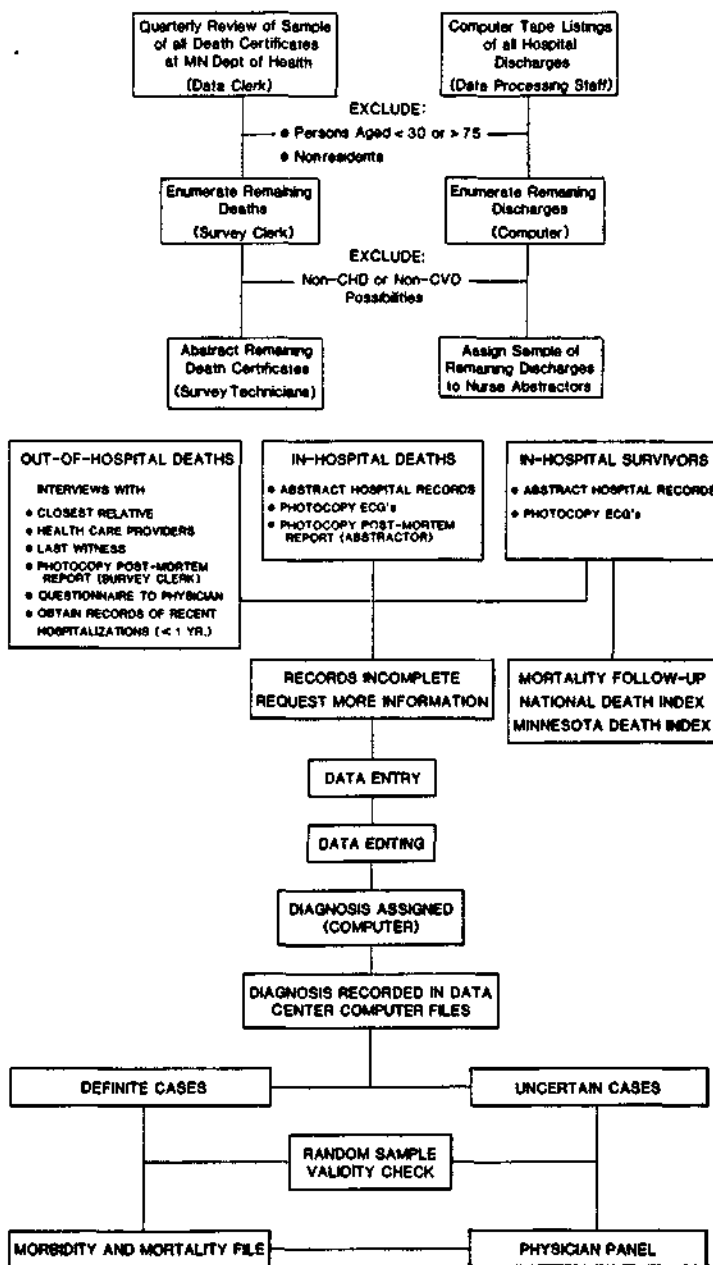


Fig. 1. Case finding and diagnosis validation of hospitalized cases of acute myocardial infarction and acute stroke and coronary heart disease death out of hospital.

investigators intimately involved in their development and subsequent use in these trials. In addition, criteria used in community surveillance studies in the United States and those of the WHO myocardial infarction and stroke registers¹⁴ were reviewed. A dialogue was maintained with a WHO working group, who were updating the WHO myocardial infarction register system. Drafts of the criteria were circulated to experts in the epidemiology and clinical diagnosis of myocardial infarction and stroke. At several points in the process the criteria were pilot

tested on case records from the Framingham Cardiovascular Disease Survey files, as well as on cases from hospitals cooperating in current research efforts. This led to further revisions. Finally, in a rigorous test of their logic, the criteria were reduced to algorithms suitable for translation into a computer program for assigning diagnoses. Many further revisions resulted from this process, as flaws in the logic became evident. The aim was to make the criteria so explicit that the exercise of clinical judgment would be necessary in only a small fraction of

difficult cases. The criteria have now been applied to over 5,000 cases by the Minnesota Heart Survey, Stanford Five City Project, and other programs. The criteria are included in test form as Appendix 1. They are presented in tabular form in Appendix 2 (available upon request from authors). Some illustrative cases are included as Appendix 3 (available on request from authors).

It is vital that the data to which the criteria are applied be collected in a standardized way. The following is a description of the proposed case-finding process and the data set to be collected. The case-finding process used by the Minnesota Heart Survey is diagrammed in Fig. 1. The investigators must carefully define the population at risk by specifying its age limits and its geographic limits as determined by place of usual residence. It is not feasible to routinely validate all hospitalized cases of illness in a community. A list of ICD-9-CM discharge diagnosis codes is proposed here to ascertain nearly all cases in which a myocardial infarction or stroke might have occurred (Appendix 2). If there is reason to believe that other discharge codes may at times be used in a local situation for myocardial infarction or stroke cases these should be added to the list. After a large number of cases have been abstracted, all codes proved to yield few cases of myocardial infarction or stroke may be omitted from the list. However, to assure nearly complete ascertainment of cases, the list in Appendix 2 (available on request from the authors) is suggested as a starting point for pilot testing. All cases bearing codes of this list, either as a primary or secondary diagnosis, are to be reviewed initially.

Appendix 4 (available on request from the authors) contains data collection forms designed for use with these criteria. Defined is the minimum data set needed to apply the criteria in a reasonably comparable manner. Other data may be collected according to the needs and purpose of each study. However, if each study collects the minimum data set, it will be possible to apply the criteria and make direct interstudy comparisons of morbidity rates. This in no way prevents any study from using one or more different sets of criteria, which may use more or less data than the minimum data set suggested. Appendix 5 (available on request from the authors) presents preliminary results of analyses of data availability, and to the validity and repeatability of diagnoses assigned by these criteria.

CONCLUSIONS

The use of the outlined surveillance procedures and the current criteria with necessary modifications will facilitate interstudy and longitudinal com-

parisons of cases and morbidity rates and will reduce bias arising from differing methods of case ascertainment, validation, and diagnostic criteria. The availability of such comparable data will be a major advance in the epidemiologic study of geographic and longitudinal variation in cardiovascular morbidity and mortality.

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APPENDIX 1

CRITERIA FOR EVENTS

The events will be classified as definite, possible, and no event.

I. Fatal coronary events

A. Definite fatal myocardial infarction (MI) (Dx code 01)

- 1a. Definite MI within 4 weeks of death by criteria (see below for criteria for definite MI)

-OR-

- 1b. Acute MI diagnosed by autopsy

-AND-

2. No known nonatherosclerotic or noncardiac-atherosclerotic process that was probably lethal according to death certificate, autopsy report, hospital records, or physician records.

B. Definite sudden death due to coronary heart disease (CHD) (Dx code 02)

1. Death witnessed as occurring within 1 hour after the onset of severe cardiac symptoms (prolonged cardiac pain—see below, shortness of breath, fainting) or within 1 hour after the subject was last seen without symptoms

-AND-

2. No documentation of definite acute MI within 4 weeks prior to death by criteria (see below for criteria for definite MI)

-AND-

3. No known nonatherosclerotic or noncardiac-atherosclerotic process that was probably lethal according to death certificate, autopsy report, hospital records, or physician report.

C. Definite fatal CHD (DX code 03)

1. Death certificate with consistent underlying or immediate cause(s) (ICD-9 codes 410-414)

-AND-

2. No documentation by criteria of definite acute MI within 4 weeks prior to death

-AND-

3. Criteria for sudden death not met

-AND-

4. No known nonatherosclerotic or noncardiac-atherosclerotic process or event that was probably lethal according to death certificate, autopsy report, hospital records, or physician records

-AND-

- 5a. Previous history of MI according to relative, physician, or hospital records, or definite or possible MI by criteria (see below)

-OR-

- 5b. Autopsy reporting severe atherosclerotic-coronary artery disease or old MI without acute MI (>50% proximal narrowing of two major vessels or >75% proximal narrowing of one more vessel if anatomic details given)

-OR-

- 5c. Rapid death:

Death occurring greater than 1 and less than or equal to 24 hours after the onset of severe cardiac symptoms or after subject was last seen without symptoms.

D. Possible fatal CHD (Dx code 08)

1. No documentation by criteria of definite acute MI within 4 weeks prior to death

-AND-

2. No documentation by criteria of definite sudden death

-AND-

3. No documentation by criteria of definite fatal CHD

-AND-

4. Death certificate with consistent underlying or immediate cause (ICD-9 codes 410-414)

-AND-

5. No known nonatherosclerotic or noncardiac-atherosclerotic process that was probably lethal according to death certificate, autopsy report, hospital records, or physician records.

II. Nonfatal MI

A. Definite (Dx code 04)

1. Evolving diagnostic ECG

-AND/OR-

2. Diagnostic ECG and abnormal enzymes

-AND/OR-

3. Prolonged cardiac pain and abnormal enzymes.

B. Possible—one or more of the following categories using the stated definitions below (Dx code 10):

1. Equivocal enzymes and equivocal ECG (with or without pain).

2. Equivocal enzymes and diagnostic ECG (no pain).

3. Abnormal enzymes and other ECG (no pain).

4. Abnormal enzymes and equivocal ECG (no pain).

5. Abnormal enzymes alone (no pain, ECG absent or uncodable).

6. Prolonged cardiac pain and equivocal enzymes (ECG absent or uncodable).
7. Prolonged cardiac pain and equivocal ECG (enzymes incomplete).
8. Prolonged cardiac pain and diagnostic ECG (equivocal or incomplete enzymes).
9. Prolonged cardiac pain alone (ECG and enzymes incomplete).
10. Prolonged cardiac pain, "other" ECG, equivocal enzymes.
11. Prolonged cardiac pain, "other" ECG, incomplete enzymes.

Definitions

Prolonged cardiac pain: When it is characterized by pain with the following characteristics.

- (a) Occurring anywhere in the anterior chest, left arm, or jaw, which may also involve the back, shoulder, right arm, or abdomen on one or both sides.
- (b) Duration of more than 20 minutes.

ECG

- (a) *Evolving diagnostic ECG*—an evolving pattern on serial ECGs of a diagnostic ECG. (An evolving pattern of changes [appearance or disappearance within lead groups: anterior (V₁-V₃); lateral (I, aV_L, V₆); inferior (II, III, aV_F)] establishes the infarct as acute. Two or more ECG recordings during the hospitalization are needed for this classification.)

- (1) No Q code in one ECG record followed by a record with a *diagnostic Q* code (Minn. code 1-1-1 through 1-2-5 plus 1-2-7)

-OR-

- (2) An equivocal Q code (Minn. code 1-2-8 or any 1-3 code) and no major ST segment depression in one ECG record followed by a record with a *diagnostic Q* code PLUS a major ST segment depression (Minn. code 4-1, or 4-2)

-OR-

- (3) An *equivocal Q* code and no ST segment elevation in one ECG record followed by a record with a *diagnostic Q* code PLUS an ST segment elevation (Minn. code 9-2)

-OR-

- (4) An *equivocal Q* code and no major T wave inversion in one ECG record followed by a record with a *diagnostic Q* code PLUS a major T wave inversion (Minn. code 5-1 or 5-2)

-OR-

- (5) No Q code and neither Minn. code 4-1 nor 4-2 followed by a record with an equivocal Q code plus a 4-1 or a 4-2

-OR-

- (6) No Q code and no Minn. code 9-2 followed by a record with an equivocal Q-code plus a 9-2

-OR-

- (7) No Q code and neither Minn. code 5-1 nor 5-2 followed by a record with an equivocal Q code plus a 5-1 or a 5-2.

(b) *Diagnostic ECG.*

- (1) Minn. code 1-1-1 through 1-2-5 and 1-2-7 for diagnostic Q and QS patterns

-OR-

- (2) Minn. code 9-2 for ST segment elevation PLUS any T wave depression item coded 5-1 or 5-2

(none of the above T wave depression items can be used in the presence of ventricular conduction defects).

(c) *Equivocal ECG.*

- (1) Q and QS pattern Minn. code 1-2-8 through 1-3-6

-OR-

- (2) ST junction (J) and segment depression Minn. code 4-1 through 4-3

-OR-

- (3) T wave items Minn. Code 5-1 through 5-3

-OR-

- (4) ST segment elevation item Minn. code 9-2.

(d) *Other ECG:* all other findings, including normal.(e) *Uncodable ECG.*

- (1) Missing lead.
- (2) Baseline drift greater than 1 in 20, if it obscures ST-T wave.
- (3) Muscle tremor artifact giving more than 2 mm peak-to-peak oscillation.
- (4) Other technical errors making Q-wave measurement impossible, such as extreme lack of centering or marked clipping.
- (5) Major abnormal QRS conduction patterns, e.g., complete bundle branch blocks, artificially paced rhythms, etc.

(f) *Absent ECG:* No ECG available for coding.

The ECG series will be assigned the highest category for which criteria are met, i.e., evolving diagnostic > diagnostic > equivocal > other.

Cardiac enzymes

Enzymes will be considered for the category of "abnormal" only if the upper limit of normal for the laboratory making the determination is recorded for the enzyme(s) used to make the diagnosis and:

- a. CPK-MB and total CPK have been measured within 72 hours of admission or onset of acute event, whichever is later

-OR-

- b. Total CPK has been measured and one of LDH or SGOT has been measured within 72 hours of admission or onset of acute event, whichever is later.

Enzymes are "abnormal" if:

1. CPK-MB has been measured and is "present" (if hospital uses criteria of "present" and "absent") or at least twice the upper limits of normal (if hospital uses quantitative criteria) and total CPK is at least twice the upper limits of normal

-OR-

2. Total CPK has been measured and is at least twice the upper limits of normal and either LDH or SGOT has been measured and is at least twice the upper limits of normal.

Enzymes will be considered for the category of "equivocal" only if the upper limit of normal for the laboratory making the determination is recorded for the enzyme(s) used to make the diagnosis.

Enzymes are "equivocal" if:

1. CPK-MB and total CPK have been measured within 72 hours of admission or onset of acute event and CPK-MB is above the upper limits of normal for laboratories giving quantitative values or "present" for laboratories giving qualitative values but in either case total CPK is less than twice the upper limits of normal

-OR-

2. At least one of CPK, LDH, or SGOT has been measured within 72 hours of admission or onset of acute event and is above the upper limits of normal, and the criteria for "abnormal" enzymes are not met

-OR-

3. Enzymes (CPK-MB, CPK, SGOT, or LDH) are "abnormal," as defined above, but there is a nonischemic cause present (defibrillation, surgery, liver disease, injections, etc.).

Enzymes are "normal" if:

They meet criteria for consideration as "abnormal" or "equivocal" but criteria for these categories are not met.

Enzymes are "incomplete" if:

They do not meet criteria for consideration as "abnormal" or "equivocal."

III. Primary cardiac arrest with successful resuscitation

A. Definite (Dx code 07)

1. Ischemic arrest

- (a) Sudden cardiovascular (absent pulse) and pulmonary (absent spontaneous respiration) collapse with successful resuscitation

-AND-

- (b) Ventricular fibrillation or asystole reported on resuscitation ECG

-AND-

- (c) ECGs, enzymes, and history necessary for diagnosis of "definite" or "possible" MI collected. "Definite" and "possible" MI by criteria have been excluded

-AND-

- (d) No known nonatherosclerotic or noncardiac-atherosclerotic acute or chronic process or event that would have been probably lethal

-AND-

- (e) History of previous MI

-AND-

- (f) Subsequent documentation of significant CHD (but not acute MI) during same hospitalization (coronary angiography showing >50% proximal narrowing of two or more

major vessels, or >75% proximal of one or more major vessels, old MI on ECG—Minn. codes 1-1, 1-2).

2. Primary arrhythmia (without ischemia)

- (a) Sudden cardiovascular (absent pulse) and pulmonary (absent spontaneous respiration) collapse with resuscitation

-AND-

- (b) Ventricular fibrillation or asystole reported on resuscitation ECG

-AND-

- (c) ECGs, enzymes, and history necessary for diagnosis of "definite" or "possible" MI collected. "Definite" and "possible" MI by criteria have been excluded

-AND-

- (d) No known nonatherosclerotic or noncardiac-atherosclerotic acute or chronic process or event that would have been probably lethal

-AND-

- (e) No history of previous MI

-AND-

- (f) Subsequent documentation of no significant CHD during same hospitalization (absence of both >50% proximal narrowing of two or more or >75% proximal narrowing of one or more major vessels on coronary angiography).

3. Nonspecific (insufficient information to classify as ischemic or primary arrhythmia)

- (a) Sudden cardiovascular (absent pulse) and pulmonary (absent spontaneous respiration) collapse with resuscitation

-AND-

- (b) Ventricular fibrillation or asystole reported on resuscitation ECG

-AND-

- (c) ECGs, enzymes, and history necessary for diagnosis of "definite" or "possible" MI collected. "Definite" and "possible" MI by criteria have been excluded

-AND-

- (d) No known nonatherosclerotic or noncardiac-atherosclerotic acute or chronic process or event that would have been probably lethal.

B. Possible (Dx code 12)

1. Apparent sudden cardiovascular and pulmonary collapse with resuscitation as with "definite primary cardiac arrest."

-AND-

2. Lack of documentation for ventricular fibrillation or asystole during resuscitation

-AND-

3. Definite MI by criteria has not been diagnosed for this event

-AND-

4. No known nonatherosclerotic or noncardiac-atherosclerotic acute or chronic process or event that would have been probably lethal.

IV. Fatal stroke**A. Definite (Dx code 05)**

- 1a. Cerebral infarction or hemorrhage diagnosed at autopsy
-AND-

- 1b. Other disease process or event such as brain tumor, subdural hematoma, subarachnoid hemorrhage, metabolic disorder, or peripheral lesion that could cause localizing neurologic deficit or coma—according to death certificate, autopsy, hospital records, or physician records
-OR-

- 2a. History of rapid onset (approximately <48 hours from onset to time of admission or maximum acute neurologic deficit) of localizing neurologic deficit and/or change in state of consciousness
-AND-

- 2b. Documentation of localizing neurologic deficit by unequivocal physician or laboratory finding within 6 weeks of death with >24 hours duration of objective physician findings
-AND-

- 2c. See list under 1b above.

B. Possible (Dx code 09)

1. Death certificate with consistent underlying or immediate cause (ICD-9, codes 431-437)
-AND-

2. No evidence at autopsy examination of the brain, if performed, of any disease process other than cerebral infarction or hemorrhage that could cause localizing neurologic signs (see 1b above).

V. Nonfatal stroke**A. Definite (Dx code 06)**

1. History of rapid onset (approximately <48 hours from onset to time of admission or maximum acute neurologic deficit) of localizing neurologic deficit and/or change in state of consciousness
-AND-

2. Documentation of localizing neurologic deficit by unequivocal physician or laboratory finding within 6 weeks of onset with >24 hours duration of objective physician findings
-AND-

3. No other disease process or event such as brain tumor, subdural hematoma, subarachnoid hemorrhage, metabolic disorder, or peripheral lesion that could cause localizing neurologic deficit or coma according to hospital records.

B. Possible (Dx code 11)

- 1a. History of rapid onset (approximately <48 hours from onset to time of admission or maximum

acute neurologic deficit) of localizing neurologic deficit and/or change in state of consciousness
-AND-

- 1b. Documentation of localizing neurologic deficit by unequivocal physician or laboratory finding within 6 weeks of onset with >24 hours duration of objective physician findings
-OR-

- 1c. Discharge diagnoses with consistent primary or secondary codes (ICD-9-CM codes 431, 432, 434, 436, 437)
-AND-

2. No evidence by unequivocal physician or laboratory findings of any other disease process or event causing focal brain deficit or coma other than cerebral infarction or hemorrhage according to hospital records.

Unequivocal laboratory findings

1. A computerized axial tomography scan showing no definite findings of any disease process or event causing focal brain deficit or coma other than cerebral infarction or hemorrhage
-AND-

- 2a. Showing a focal area of decreased or normal attenuation consistent with cerebral infarct
-OR-

- 2b. Showing focal increased attenuation consistent with intracerebral hemorrhage.

Criteria section	Diagnostic code
I.A.	01. Definite <i>fatal</i> MI
I.B.	02. Definite <i>sudden death</i> due to CHD
I.C.	03. Definite <i>fatal</i> MI
II.A.	04. Definite <i>nonfatal</i> MI
IV.A.	05. Definite <i>fatal</i> stroke
V.A.	06. Definite <i>nonfatal</i> stroke
III.A.	07. Definite primary cardiac arrest—with resuscitation
I.D.	08. Possible <i>fatal</i> CHD
IV.B.	09. Possible <i>fatal</i> stroke
II.B.	10. Possible <i>nonfatal</i> MI
V.B.	11. Possible <i>nonfatal</i> stroke
III.B.	12. Possible primary cardiac arrest—with resuscitation
	98. <i>Fatal</i> event not due to CHD or stroke
	99. <i>Nonfatal</i> event not due to CHD or stroke

N.B. When criteria are met for two events occurring within 6 weeks of each other, the primary diagnosis will be that with the lowest diagnostic code in this hierarchy.

Criteria for Categorizing Electrocardiogram Data

At least one dated ECG must be present or the ECG will be defined as absent. Lead groups are Anterior (V1-V5), Lateral (I, aVL, V6), and Inferior (II, III, aVF).

a. Definite ECG

An evolving pattern of Q or QS changes within a lead group establishes the infarct as acute.

Two or more ECG readings during the hospitalization are needed for this classification: There are eight possible sets of serial changes defined below, any one of which is sufficient:

A. Evolving Q Waves

- (1) One ECG record showing no major Q or QS code and a later record with a diagnostic Q or QS code (Minn. code 1-1-1 through 1-2-5 and 1-2-7).
- (2) A minor Q code (1-2-8 or any 1-3 code) and no ST segment depression in one ECG followed by a later record showing a diagnostic Q code (1-1-1 through 1-2-5 plus 1-2-7) plus ST segment depression code 4-1 or 4-2).
- (3) A minor Q code and no ST segment elevation in one ECG followed by later record with a diagnostic Q code plus ST segment elevation (code 9-2).
- (4) A minor Q code and no T wave inversion in one ECG followed by a record with a diagnostic Q code plus T wave inversion (code 5-1 or 5-2).
- (5) No Q code and no ST depression (4-1, 4-2) on one ECG followed by a record with a minor Q code plus ST depression (4-1, 4-2).
- (6) No Q code and no ST elevation in one ECG followed by a record with a minor Q code and ST elevation (code 9-2).
- (7) No Q code and no T inversion in one ECG followed by a record with a minor Q code and T inversion (5-1 or 5-2).

B. Evolution of an Injury Current

- (8) An ST segment elevation (9-2) lasting more than one day and T wave progression from 5-0 or 5-4 to 5-1.

b. Probable ECG**A. Static Diagnostic Changes: either (1) or (2):**

- (1) Minnesota Code for Q and QS pattern 1-1-1 through 1-2-5 or 1-2-7 on all records; or
- (2) Minnesota Code for S-T segment elevation 9-2 plus T inversion (code 5-1 or 5-2; cannot use T wave item in presence of ventricular conduction defects).

B. Evolution of Repolarization Changes: any of the following:

- (1) No ST segment depression in one ECG record and other records with major ST segment depression (4-1).
- (2) No ST segment elevation in one ECG record and other records with ST segment elevation (9-2).
- (3) No T wave inversion in one ECG record and other records with major T wave inversion (5-1 or 5-2).

c. Equivocal ECG

Any of the following Minnesota codes:

- (1) Q and QS pattern 1-2-8 through 1-3-6;
- (2) S-T junction (J) and segment depression 4-1 to 4-3;
- (3) T wave item 5-1 through 5-3;
- (4) ST elevation code 9-2.

d. Other ECG

All other patterns, including normal will be included here.

ECG Interpretation Program

1. Get all the ECGS's for the event.
2. Do not use ECG's which do not have a date or have no codes.
3. Code those records with 9-8-1 or 8-2-1 "UNUSED" and those with 6-8 or 8-2-6 "PACER".
 - 3a. If all ECGs are coded "UNUSED" or "PACER" then code this ECG sequence "OTHER" and then STOP.
4. If an ECG is coded 6-1 , call it "AV BLOCK" and do not use.
 - 4a. If all ECGS are "AV BLOCK", code this sequence "OTHER" then STOP.
5. If an ECG is coded 7-1 or 7-6, call it "LBBB" and do not use.
 - 5a. If all ECG's are "LBBB", code sequence "OTHER" then STOP.
6. If an ECG is coded 7-4, call it "IVCD" and do not use.
 - 6a. If all ECGS are "IVCD", code sequence "OTHER" and STOP.
7. Now examine the "Anterior Lead Group" (V1,V5) of all remaining individually.
 - 7a. If only one ECG remains, go to 16 below.

CODE ALL RECORDS AS FOLLOWS:

9. Q field (1-X-X codes)
 - Qo: No 1-X-X code
 - Q1: Any 1-3-X or 1-2-8
 - Q2: Any code 1-1-1 through 1-2-5 or 1-2-7
9. STD field (4-X codes)
 - STDo: No 4-X code or 4-3 or 4-4
 - STD1: 4-2
 - STD2: 4-1
10. T field (5-X codes)
 - To: No 5-X or 5-4
 - T1: 5-3
 - T2: 5-2
 - T3: 5-1
11. STE field (9-X codes)
 - STEO: No 9-2
 - STE1: 9-2

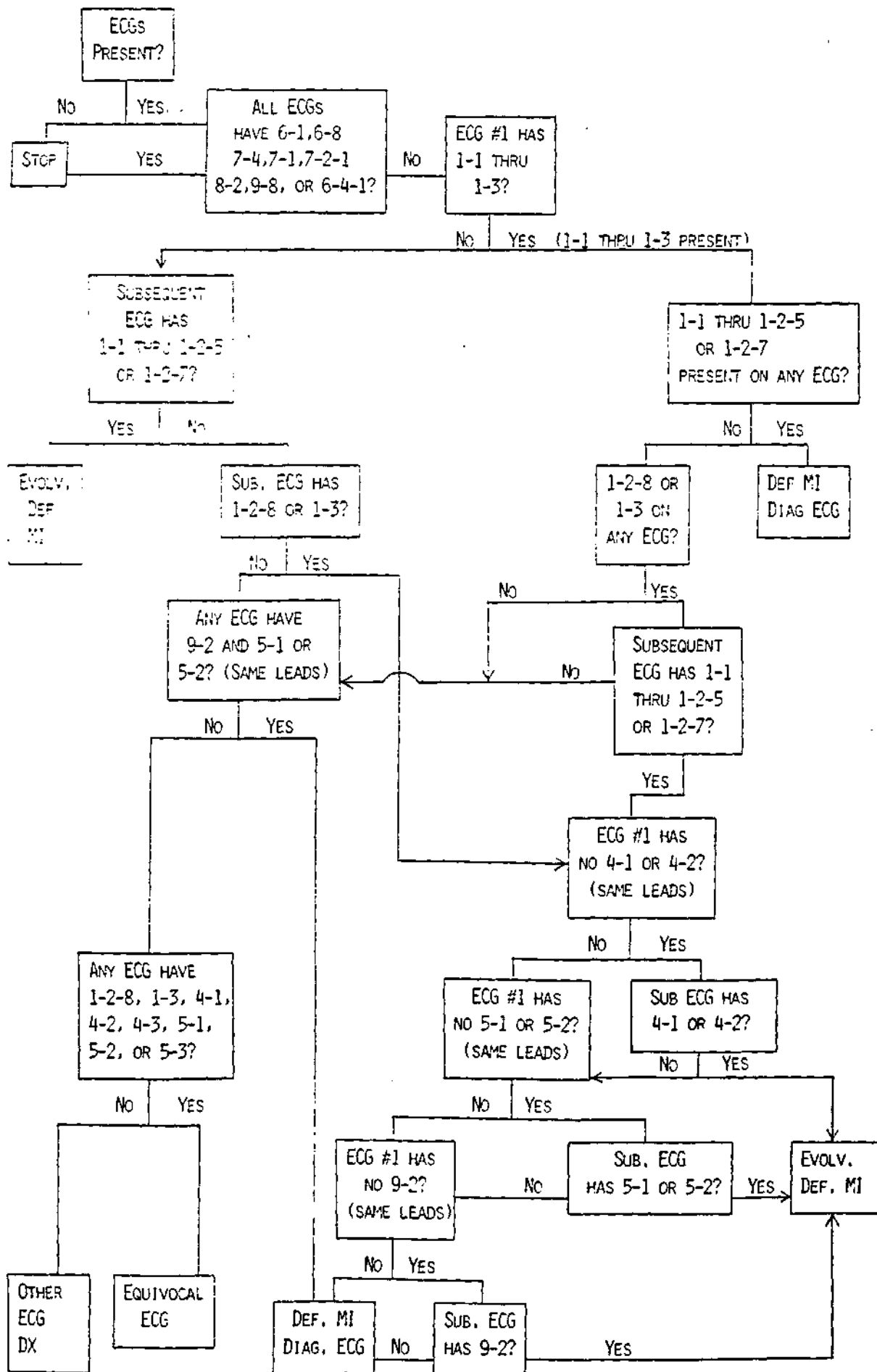
Repeat steps 12-13 for Anterior Lead Group, Lateral Lead Group, and Inferior Lead Group if a code has not been reached for the previous lead group. If at the end of all lead groups a code has not been reached go to 15.

12. Lead group sequence coding:

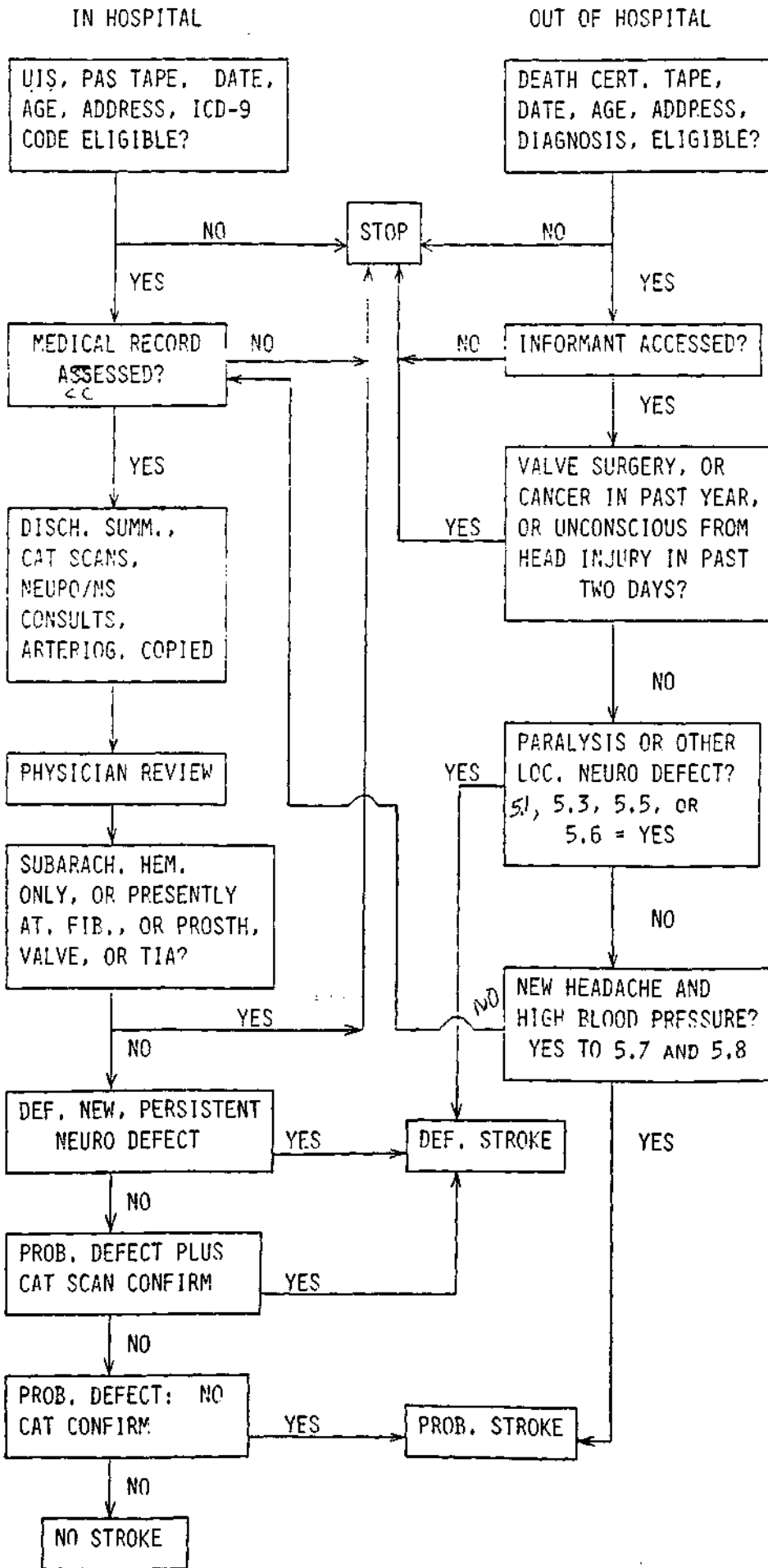
- 12a. Is there any Qo followed by any Q2? YES: go to 12h
NO : go to 12b
- 12b. Is there a Q1STDo followed by a Q2STD1 or Q2STD2? YES: go to 12h

- 12c. Is there a Q1To followed by a Q2T2 or Q2T3? NO : go to 12c
YES: go to 12h
- 12d. Is there a Q1STEO followed by a Q2STE1? NO : go to 12d
YES: go to 12h
- 12e. Is there a QoSTDo followed by a Q1STD1 or Q1STD2? NO : go to 12e
YES: go to 12h
- 12f. Is there a QoTo followed by a Q1T2 or Q1T3? NO : go to 12f
YES: go to 12h
- 12g. Is there a QoSTEO followed by a Q1STE1? NO : go to 12g
YES: go to 12h
- 12h. Does any Qo record appear following a Q1 or Q2 record? NO : go to 13
YES: code "CODING INCONSISTENT" then STOP
NO : code "DEFINITE ECG A" then STOP
13. Are there two records more than 24 hours apart but YES: continue
within 5 days of the event? NO : go to 14
- Are there two records on different days with STE1? YES: go to 13a
NO: go to 14
- 13a. Is there a record with To followed by a record YES: DEFINITE ECG B
with T3? STOP
NO : go to 14
14. Repeat steps 8-13 for "Lateral Lead Group" (1,L,V6);
if read "go to 14", then repeat steps 8-13 for "Inferior Lead Group"
(2,3,F); if again reach "go to 14" then go to 15.
15. Examine "Anterior Lead Group" sequence:
- 15a. Is there a record with STD2 and another YES: PROBABLE ECG B, STOP
record with STDo (temporal order irrelevant)? NO : go to 15b
- 15b. Is there a record with STE1 and another YES: PROBABLE ECG B, STOP
record with STEo (sequence irrelevant)? NO : go to 15c
- 15c. Is there a record with To and another YES: PROBABLE ECG B, STOP
record with T2 or T3 (sequence irrelevant)? NO : go to 15d
- 15d. Repeat 15a through 15c for Lateral and go to 16
Inferior Lead Groups; if reach "go to 15d",
16. Examine all available records:
- 16a. Does any record have Q2? YES: PROBABLE ECG A, STOP
NO : go to 16b
- 16b. Does any record have STE1 plus T2 or T3? YES: PROBABLE ECG A, STOP
NO: go to 16c
- 16c. Does any record have Q1 or STD1 or STD2 or YES: EQUIVOCAL, STOP
code 4-3 or T1 or T2 or T3 or STE1? NO: OTHER, STOP

DEFINITE MI BY ECG



PHHP MORBIDITY AND MORTALITY
SURVEILLANCE FOR STROKE





Surveillance

CORE DATA SHEET

CDS #: _____

Hospital I.D.: _____

Chart #: _____

Study I.D. _____

Discharge Date: _____

Admission Date: _____

Case Disposition: _____

Discharge Diagnoses 1-7: _____

1. Folder No. (If different from Chart #): _____

2. First three letters of patient's last name: _____

3. First letter of patient's first name: _____

4. Social Security No.: _____
(Enter "9" in all boxes if not recorded)

HOURS MINUTES

5. Time of Admission: _____

1. A.M.

2. P.M.

6. Marital Status:

1. NEVER MARRIED

2. MARRIED

3. SEPARATED

4. DIVORCED

5. WIDOWED

9. NR

7. Occupation Status (current):

1. RETIRED

2. NOT WORKING
(DISABLED)

3. NOT WORKING
(OTHER)

4. HOMEMAKER

5. STUDENT

6. EMPLOYED
FT OR PT (SPECIFY OCCUPATION) _____

9. NR

8. Veteran:

1. NO

2. YES

9. NR

9. Physician discharge diagnoses as found in the Medical Record:

a. Primary: _____

b. Other: _____

c. Other: _____

d. Other: _____

e. Other: _____

f. Other: _____

g. Other: _____

ACCESS RECORD

Instruments Included in Packet:

M.I. ABTRACTOR I	1.	NO	2.	YES	_____
M.I. ABSTRACTOR II	1.	NO	2.	YES	_____
AUTOPSY	1.	NO	2.	YES	_____
STROKE	1.	NO	2.	YES	_____

Record for all attempts:

Access Attempts	Date	Length of Time (in min.)	Abst. I.D.	DISP.	NOTES
1.					
2.					
3.					
4.					
5.					

10. Record the following for the last attempt:

A. NUMBER OF ACCESSES:

B. LAST ABSTRACT DATE:

(year, month, day)

11. Record the total length of time for location and abstraction in minutes, adding time from all attempts.

12. Abstractor I.D.:

13. Transcriber I.D.:

14. Abstraction Disposition:

FOR ALL 410's AND 411's, AND FATAL 412-414, 786.5's - CONTINUE ABSTRACTION.

FOR ICD-9 DISCHARGE CODES 412, 413, 414 and 786.5

THAT ARE NON-FATAL CASES:

According to the Discharge Summary and/or the E.R. Sheet:

1. Were there complaints of pain, heaviness or discomfort, including severe shortness of breath?

NO YES

2. Was there any evidence of unexplained unconsciousness before or after admission?

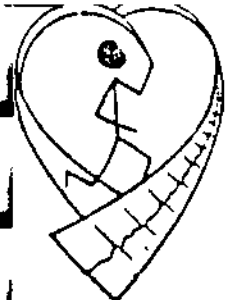
NO YES

3. Were there any new occurrences of ventricular tachycardia, ventricular fibrillation or frequent premature ventricular contractions/impulse (PVCs, PVTs)?

NO YES

1. IF NO TO ALL
ABOVE - STOP
FDX = NON EVENT

2. IF YES TO ONE OR
MORE CONTINUE
ABSTRACTION



Surveillance

Version 26
9/26/84

MYOCARDIAL INFARCTION ABSTRACT 1

CDS #: _____

Hospital ID: _____

Chart #: _____

Study ID: _____

Discharge Date: _____

Admission Date:

Case Disposition:

Discharge Diagnoses 1-7:

Abstractor Code:

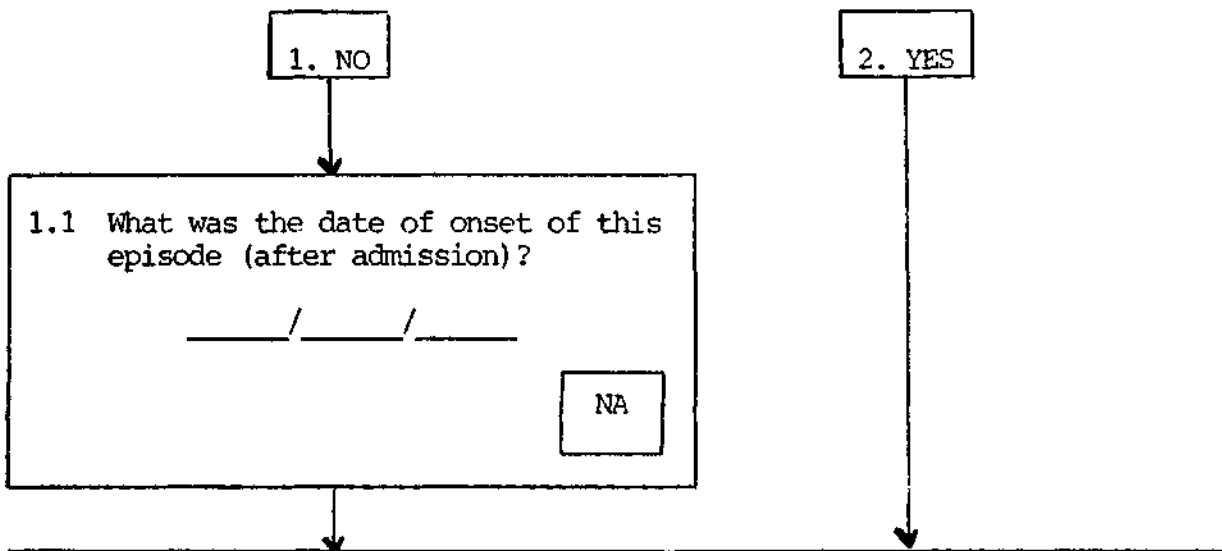
Date Abstracted: ____/____/____

IF TRANSFER

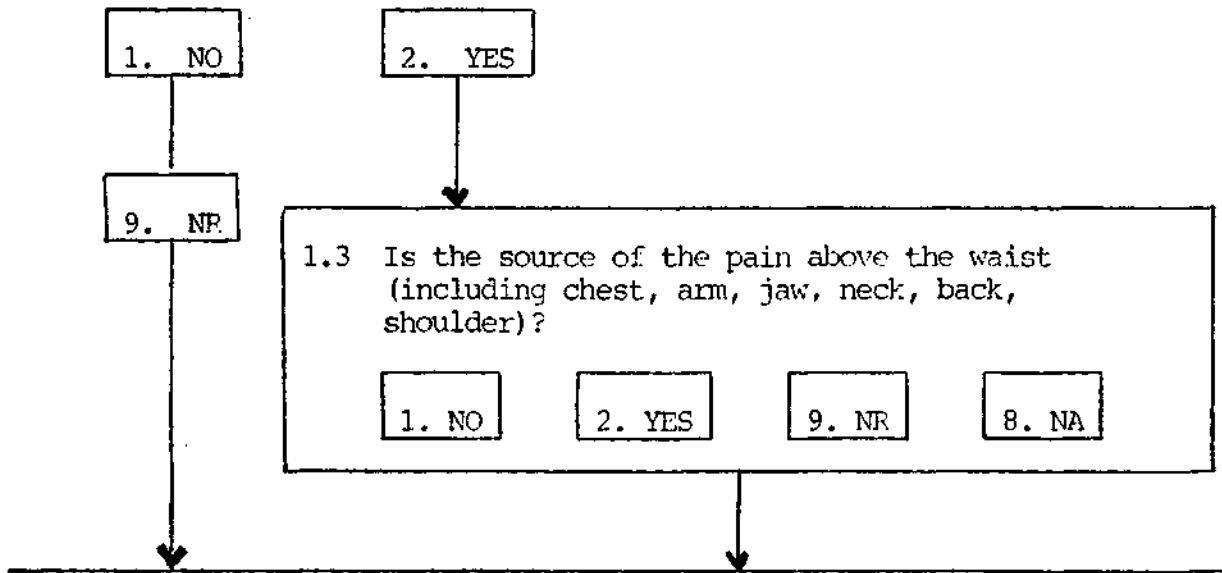
Transcriber Code:

(NA = 88)

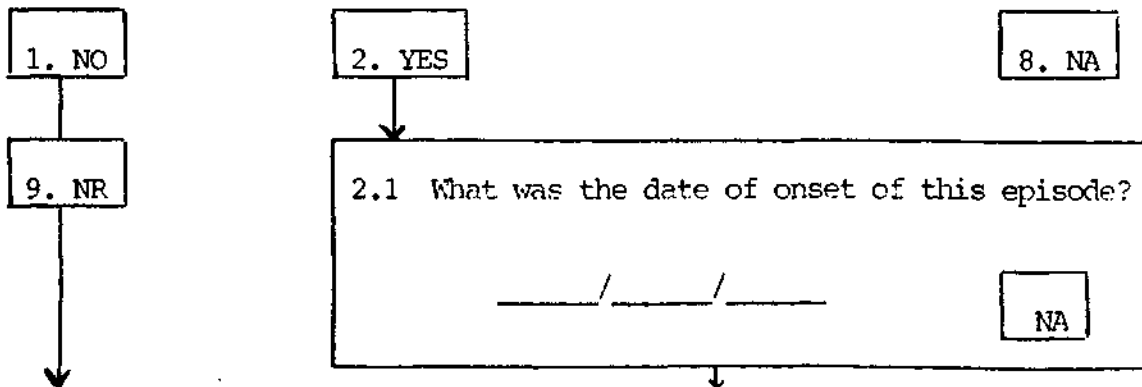
1. Did the onset of the first cardiac episode begin on or before the time of admission? (Either prior to presentation at the hospital or in the ER)?



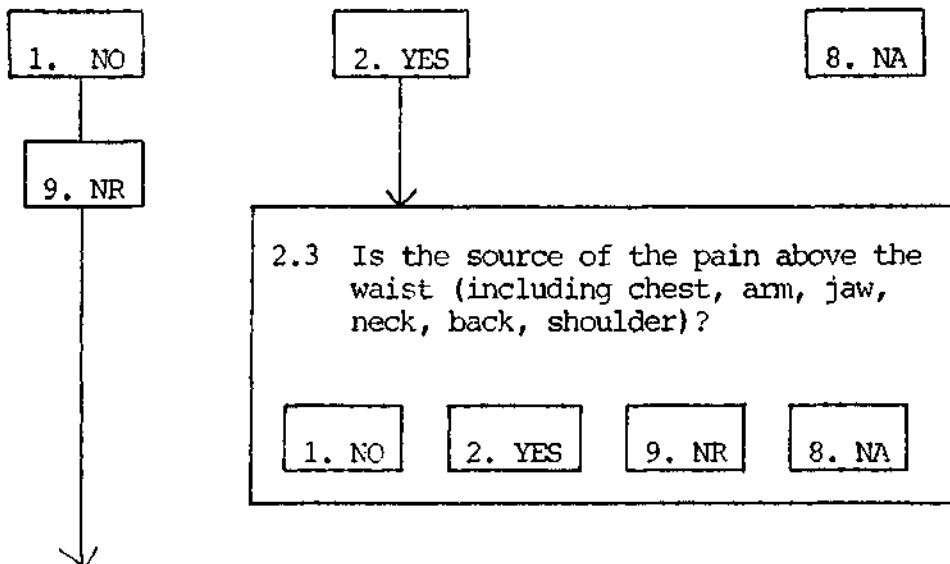
1.2 Was there any complaint of pain, heaviness, or discomfort associated with this episode?



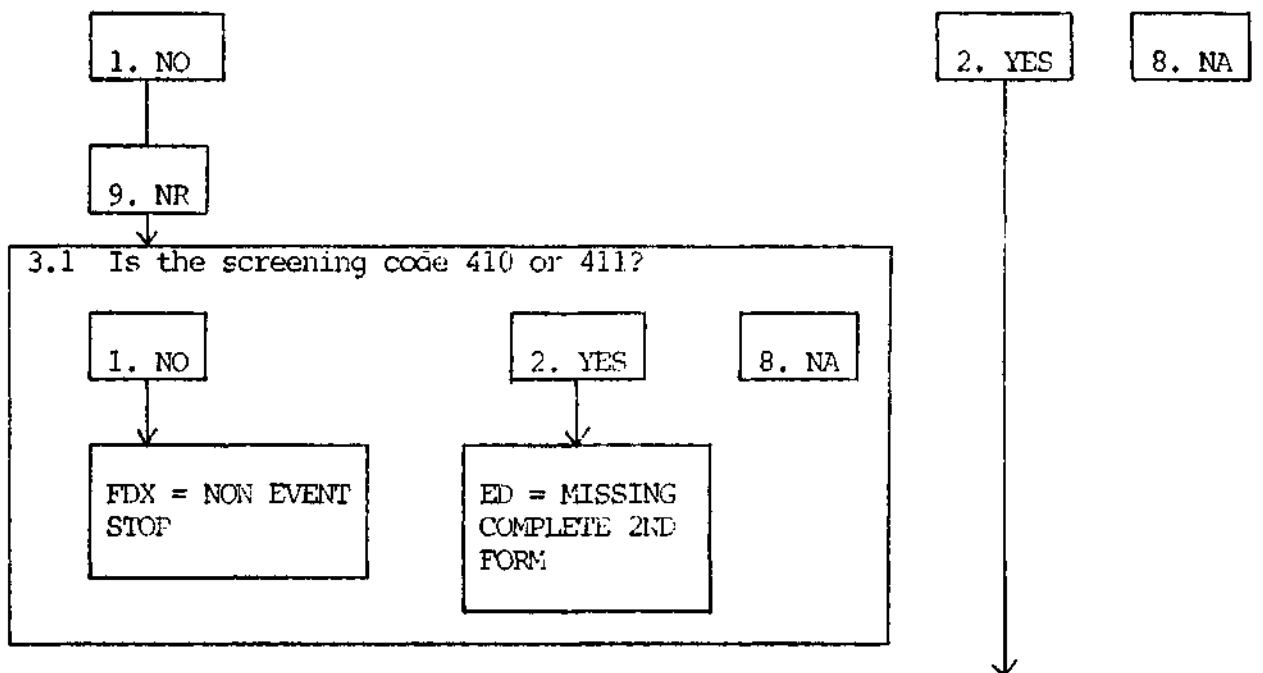
2. Was there a second cardiac episode during this admission?



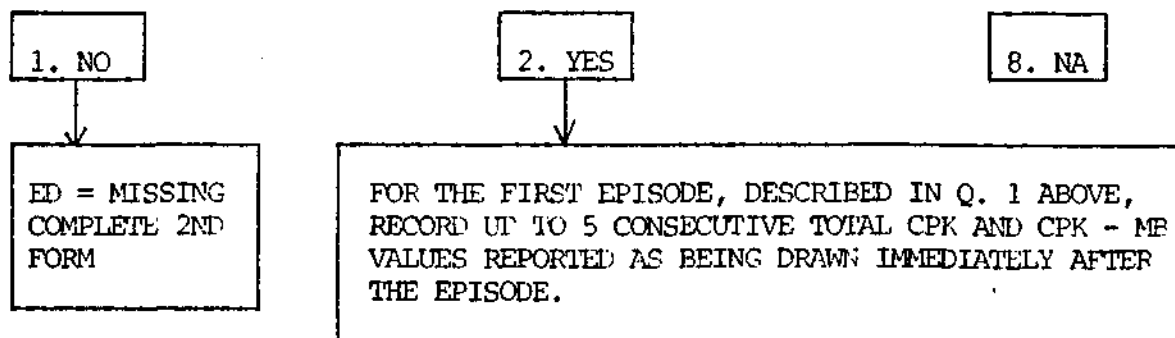
2.2 Was there any complaint of pain, heaviness, or discomfort associated with this episode?



3. Were any Total CPK levels recorded?



4. Is the UIN available for at least one Total CPK value?



EPISODE 1 TOTAL CPK:

DATE	TIME	ULN	2 x ULN	RECORDED VALUE
5.1 ___/___/___	___:___	<input type="text"/>	<input type="text"/>	<input type="text"/>

5.2 ___/___/___	___:___	<input type="text"/>	<input type="text"/>	<input type="text"/>
-----------------	---------	----------------------	----------------------	----------------------

5.3 ___/___/___	___:___	<input type="text"/>	<input type="text"/>	<input type="text"/>
-----------------	---------	----------------------	----------------------	----------------------

5.4 ___/___/___	___:___	<input type="text"/>	<input type="text"/>	<input type="text"/>
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5.5 ___/___/___	___:___	<input type="text"/>	<input type="text"/>	<input type="text"/>
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EPISODE 1 CPK - MB:

6.1 / / :
 DATE TIME

1. AM IF IU/L: [][][][]
2. PM IF PERCENT: [][][]

(NA = 8's)
(NR = 9's)

IF QUALITATIVE: 1. ABSENT 2. TRACE 3. PRESENT 9. NR 8. NA

6.2 / / :
 DATE TIME

1. AM IF IU/L: [][][][]
2. PM IF PERCENT: [][][]

(NA = 8's)
(NR = 9's)

IF QUALITATIVE: 1. ABSENT 2. TRACE 3. PRESENT 9. NR 8. NA

6.3 / / :
 DATE TIME

1. AM IF IU/L: [][][][]
2. PM IF PERCENT: [][][]

(NA = 8's)
(NR = 9's)

IF QUALITATIVE: 1. ABSENT 2. TRACE 3. PRESENT 9. NR 8. NA

6.4 / / :
 DATE TIME

1. AM IF IU/L: [][][][]
2. PM IF PERCENT: [][][]

(NA = 8's)
(NR = 9's)

IF QUALITATIVE: 1. ABSENT 2. TRACE 3. PRESENT 9. NR 8. NA

6.5 / / :
 DATE TIME

1. AM IF IU/L: [][][][]
2. PM IF PERCENT: [][][]

(NA = 8's)
(NR = 9's)

IF QUALITATIVE: 1. ABSENT 2. TRACE 3. PRESENT 9. NR 8. NA

EPISODE 2:

FOR THE SECOND EPISODE (IF ANY) DESCRIBED IN Q.2 ABOVE, RECORD UP TO 5 CONSECUTIVE TOTAL CPK AND CPK-MB VALUES AS FOR EPISODE 1 ABOVE.

<u>TOTAL CPK:</u>	<u>DATE</u>	<u>TIME</u>	<u>ULN</u>	<u>2 x ULN</u>	<u>RECORDED VALUE</u>	---	---	---
7.1	___/___/___	___:___	<input type="text"/>	<input type="text"/>	<input type="text"/>			

7.2	___/___/___	___:___	<input type="text"/>	<input type="text"/>	<input type="text"/>			
-----	-------------	---------	----------------------	----------------------	----------------------	--	--	--

7.3	___/___/___	___:___	<input type="text"/>	<input type="text"/>	<input type="text"/>			
-----	-------------	---------	----------------------	----------------------	----------------------	--	--	--

7.4	___/___/___	___:___	<input type="text"/>	<input type="text"/>	<input type="text"/>			
-----	-------------	---------	----------------------	----------------------	----------------------	--	--	--

7.5	___/___/___	___:___	<input type="text"/>	<input type="text"/>	<input type="text"/>			
-----	-------------	---------	----------------------	----------------------	----------------------	--	--	--

EPISODE 2 CPK - MB:

8.1 / / :
 DATE TIME

1. AM IF IU / L: [][][][]
2. PM IF PERCENT: [][][]

(NA = 8's)
(NR = 9's)

IF QUALITATIVE: 1. ABSENT 2. TRACE 3. PRESENT 9. NR 8. NA

8.2 / / :
 DATE TIME

1. AM IF IU / L: [][][][]
2. PM IF PERCENT: [][][]

(NA = 8's)
(NR = 9's)

IF QUALITATIVE: 1. ABSENT 2. TRACE 3. PRESENT 9. NR 8. NA

8.3 / / :
 DATE TIME

1. AM IF IU / L: [][][][]
2. PM IF PERCENT: [][][]

(NA = 8's)
(NR = 9's)

IF QUALITATIVE: 1. ABSENT 2. TRACE 3. PRESENT 9. NR 8. NA

8.4 / / :
 DATE TIME

1. AM IF IU / L: [][][][]
2. PM IF PERCENT: [][][]

(NA = 8's)
(NR = 9's)

IF QUALITATIVE: 1. ABSENT 2. TRACE 3. PRESENT 9. NR 8. NA

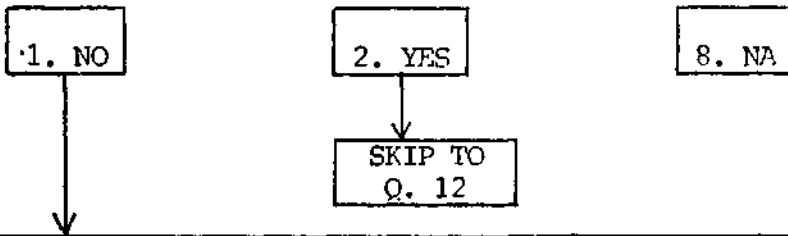
8.5 / / :
 DATE TIME

1. AM IF IU / L: [][][][]
2. PM IF PERCENT: [][][]

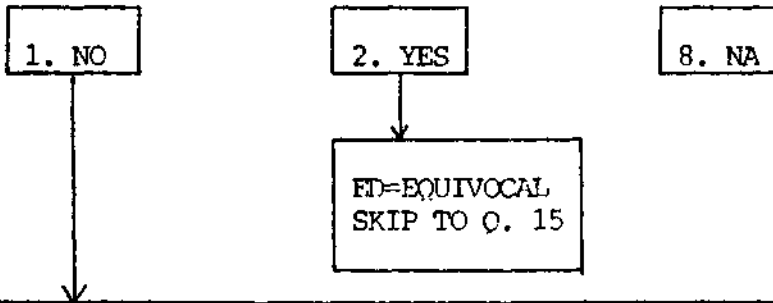
(NA = 8's)
(NR = 9's)

IF QUALITATIVE: 1. ABSENT 2. TRACF 3. PRESENT 9. NR 8. NA

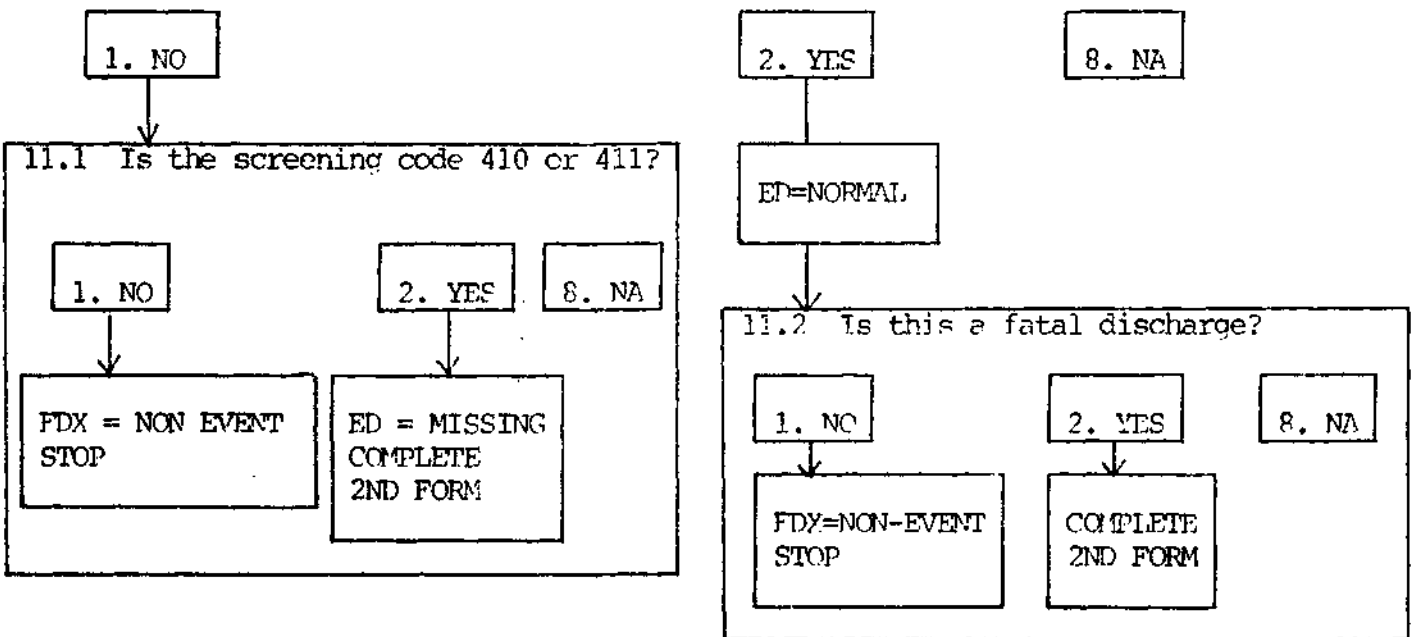
9. Is at least one CPK value \geq 2ULN?



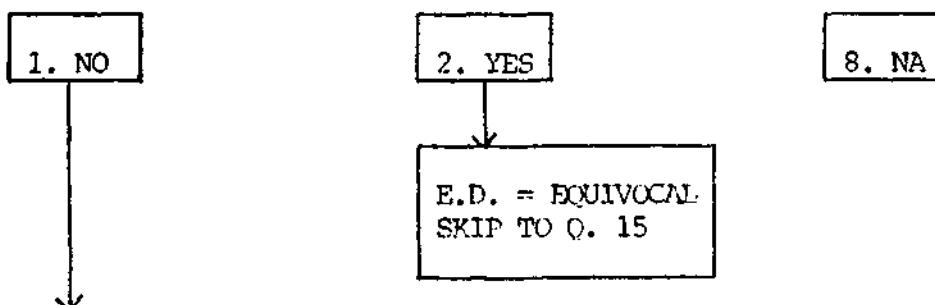
10. Is at least one CPK value \geq ULN?



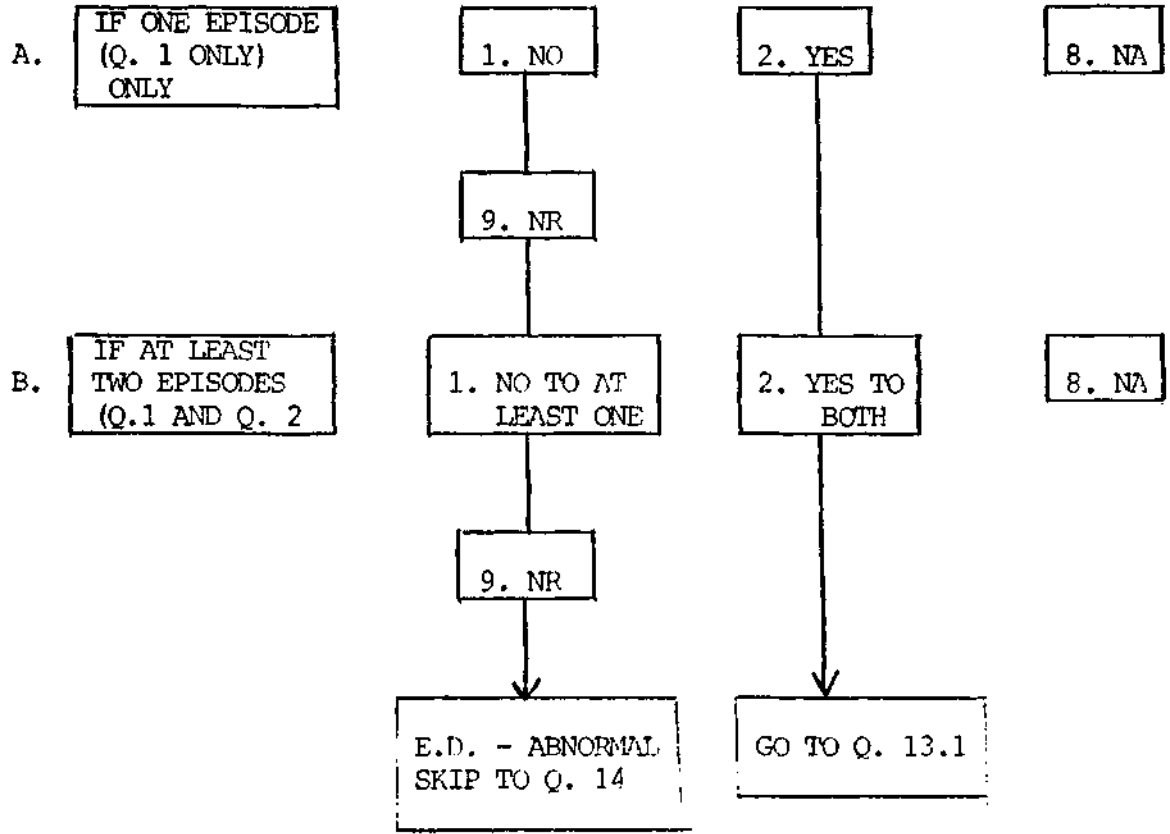
11. Are at least two CPK values available in the 96 hour period after each of the episodes defined in Q. 1 and Q. 2 above?



12. Is any form of muscle disease (ICD-9 codes 710.3, 710.4, 725, 728.0) recorded in discharge summary as present?



13. With reference to the episode(s) defined in Q. 1 and Q. 2:
 in the 72 hour period immediately prior to any CPK value \geq 2U/LN were any
 surgical procedures performed? (COMPLETE A OR B, NOT BOTH, AND CHECK NA
 FOR THE ALTERNATIVE WHICH DOES NOT APPLY.)



13.1 Record all procedures (within the 72 hour time frame of Q. 13) listed in the record using ICD-9 codes. If no ICD-9 codes are recorded, write the name of the procedure.

PROCEDURE DATE TIME

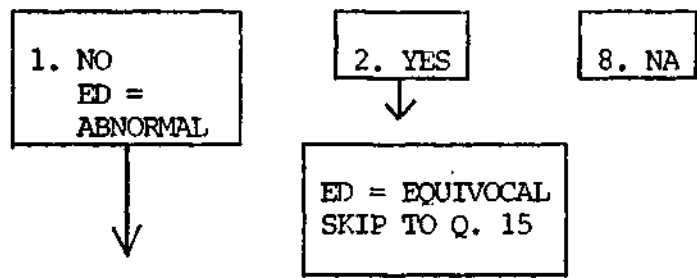
a. _____ /_____/_____ :_____

b. _____ /_____/_____ :_____

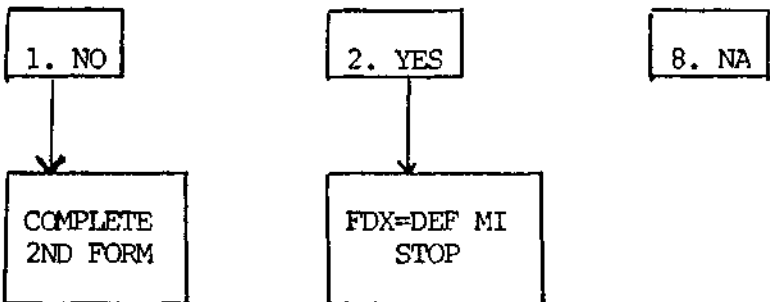
c. _____ /_____/_____ :_____

d. _____ /_____/_____ :_____

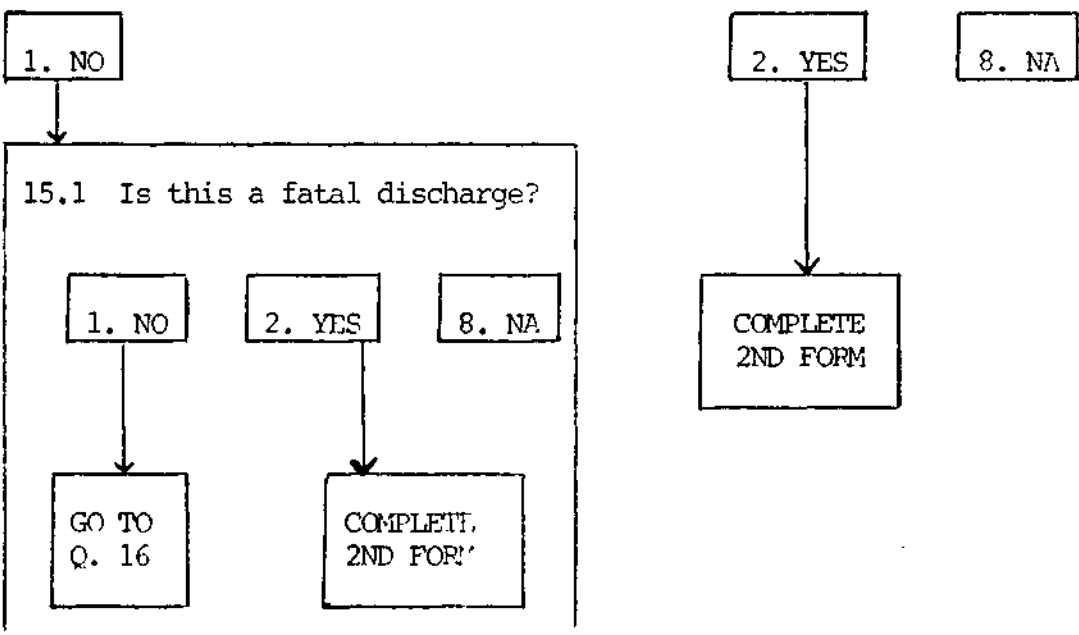
13.2 Do any procedures listed in Q. 13.1 above correspond to any on the EXCLUSION LIST?



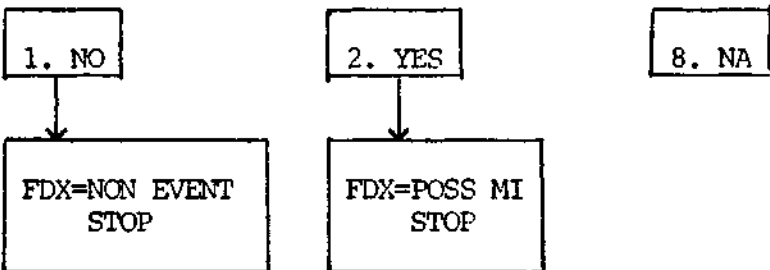
14. Is the screening code 410-411?



15. (ALL EQUIVOCALS: Q's 10, 12, 13.2)
Is the screening code 410 or 411 (see label)?



16. Is pain present (YES ON Q. 1.3 or 2.3)?





Surveillance

Version 18
09/26/84

MYOCARDIAL INFARCTION ABSTRACT II

CDS #: _____

Hospital ID: _____

Chart #: _____

Study ID: _____

Discharge Date: _____

Admission Date:

Case Disposition:

Discharge Diagnoses 1-7:

Abstractor Code:

Date Abstracted: ____/____/____

IF TRANSFER

Transcriber Code:

(NA = 88)

1. What type of admission was this? (Check 'YES' to all that apply.)

	NO	YES
a. Elective	<input type="checkbox"/>	<input type="checkbox"/>
b. Emergency	<input type="checkbox"/>	<input type="checkbox"/>
c. Transfer	<input type="checkbox"/>	<input type="checkbox"/>

1.1 From where?

1. SHORT-STAY HOSPITAL	2. NURSING HOME	3. PSYCHIATRIC INSTITUTION
4. OTHER, SPECIFY:		8. NA
9. NR		

2. REFER TO THE FIRST EPISODE (PART I Q. 1)

a. First temperature recorded after onset of first episode:

NR = .
 NA = 8 8 8 8

1. F 2. C 8. NA 9. NR

1. O 2. R 3. A 8. NA 9. NR

b. Temperature recorded 72° after onset (or nearest after 72°)

NR = .
 NA = 8 8 8 8

1. F 2. C 8. NA 9. NR

1. O 2. R 3. A 8. NA 9. NR

c. First blood pressure recorded after onset of first episode:

	SYSTOLIC	DIASTOLIC
NR =	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>
NA =	8 8 8	8 8 8

3. REFER TO THE SECOND EPISODE (IF ANY) (PART I Q. 2)

a. First temperature recorded after onset of second episode:

NR = .
 NA = 9 9 9 9
 8 8 8 8

1. F 2. C 8. NA 9. NR

1. O 2. R 3. A 8. NA 9. NR

b. Temperature recorded 72° after onset (or nearest after 72°)

NR = .
 NA = 9 9 9 9
 8 8 8 8

1. F 2. C 8. NA 9. NR

1. O 2. R 3. A 8. NA 9. NR

c. First blood pressure recorded after onset of second episode:

	SYSTOLIC	DIASTOLIC
	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>
NR =	9 9 9	9 9 9
NA =	8 8 8	8 8 8

PRE-ADMISSION HISTORY

	NO	YES	POSSIBLE	NR
4. History of coronary bypass surgery?	<input type="text"/> 1	<input type="text"/> 2	<input type="text"/> 3	<input type="text"/> 9
5. History of atrial fibrillation or flutter?	<input type="text"/> 1	<input type="text"/> 2	<input type="text"/> 3	<input type="text"/> 9
6. History of mitral stenosis?	<input type="text"/> 1	<input type="text"/> 2	<input type="text"/> 3	<input type="text"/> 9
7. History of congestive heart failure?	<input type="text"/> 1	<input type="text"/> 2	<input type="text"/> 3	<input type="text"/> 9
8. History of hypertension?	<input type="text"/> 1	<input type="text"/> 2	<input type="text"/> 3	<input type="text"/> 9
9. History of previous MI?	<input type="text"/> 1	<input type="text"/> 2	<input type="text"/> 3	<input type="text"/> 9

9.1 Date of most recent MI prior to current admission:

	MONTH	DAY	YEAR
	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
NA =	8 8	8 8	8 8
NR =	9 9	9 9	9 9

10. History of angina? NO NR YES POSSIBLE
 1 9 2 3

10.1 First attack occurred how many weeks before admission?

1. ≤ 8 WEEKS 2. > 8 WEEKS 8. NA 9. NR

11. History of cardiac arrest? NO NR YES POSS.
 1 9 2 3

11.1 Last arrest occurred how many weeks before admission?

1. ≤ 4 WEEKS 2. > 4 WEEKS ≤ 6 WEEKS

3. > 6 WEEKS ≤ 8 WEEKS 4. > 8 WEEKS 8. NA 9. NR

12. Is there evidence of any other history of cardiovascular disease in the record, other than those listed previously?

1. NO 2. YES

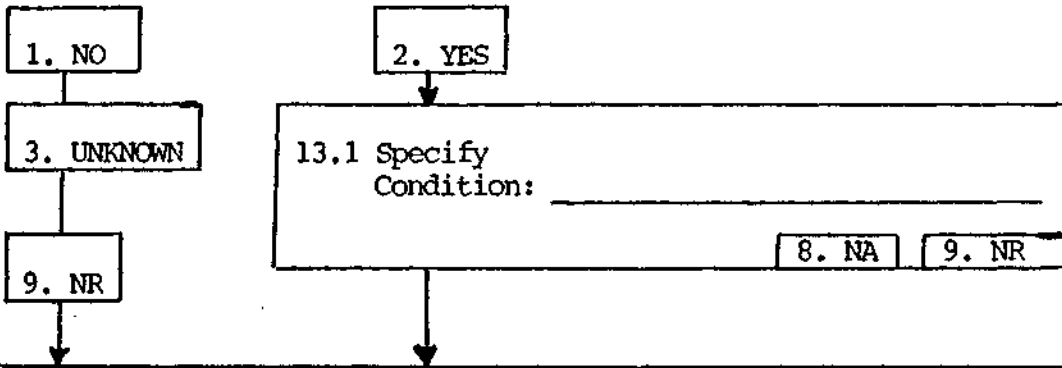
12.1 For each expression listed below, check whether or not it was mentioned in the record.

	NO	YES	POSSIBLE	NA	NR
a. CVD	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 8	<input type="checkbox"/> 9
b. ASHD	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 8	<input type="checkbox"/> 9
c. CAD	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 8	<input type="checkbox"/> 9
d. Coronary Insufficiency	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 8	<input type="checkbox"/> 9
e. Heart Disease	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 8	<input type="checkbox"/> 9
f. Other	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 8	<input type="checkbox"/> 9

Specify:

8. NA 9. NR

13. Family history of heart disease, stroke or high blood pressure?



14. Current smoker?

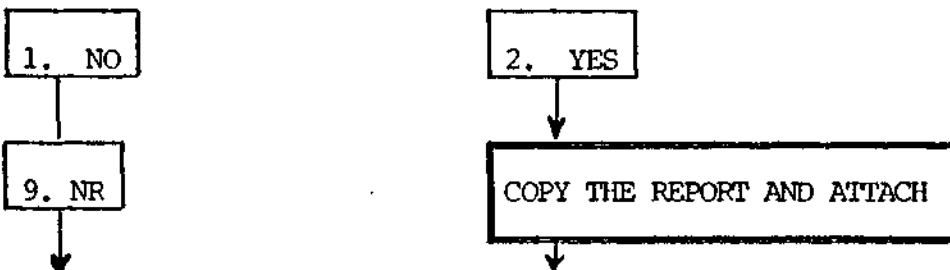
1. NO
 2. YES
 9. NR

15. Alcohol intake status:

According to the Medical Record, the patient is a: (check only one box)

1. NON-DRINKER
 2. PAST ABUSER
 3. CURRENT DRINKER
 9. NR

16. Was coronary angiography performed during this admission?



17. Were any of the following cardiac rhythm(s) documented? (check "yes" to all that apply).

	NO	YES	NR
a. Ventricular fibrillation	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 9
b. Ventricular tachycardia	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 9
c. Supraventricular tachycardia	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 9
d. Sinus tachycardia	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 9
e. Paroxysmal Atrial tachycardia (PAT)	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 9
f. Atrial fibrillation	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 9
g. Atrial flutter	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 9
h. Asystole	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 9

18. Did the patient require resuscitation at any time associated with this admission?

1. NO

2. YES

9. NR

GO TO
Q. 19

18.1 Where did the resuscitation attempts occur?

	NO	YES	NA
a. Outside the hospital	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 8
b. In the hospital, but prior to admission (in emergency room, or other hospital department)	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 8
c. I.C.U.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 8
d. C.C.U.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 8
e. Other S.C.U.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 8
f. Other hospital unit after admission	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 8

18.2 Were any of these attempt(s) unsuccessful? (i.e., patient expired)

1. NO

2. YES

8. NA

9. NR

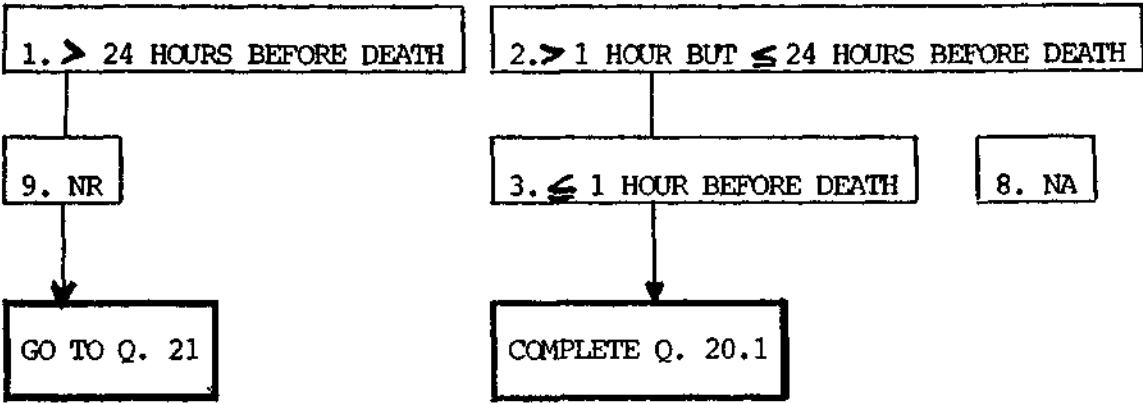
18.3 If yes, where in the hospital did the unsuccessful attempt occur?

	NO	YES	NA
In: a. I.C.U.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 8
b. C.C.U.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 8
c. Other S.C.U.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 8
d. Other hospital unit after admission	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 8

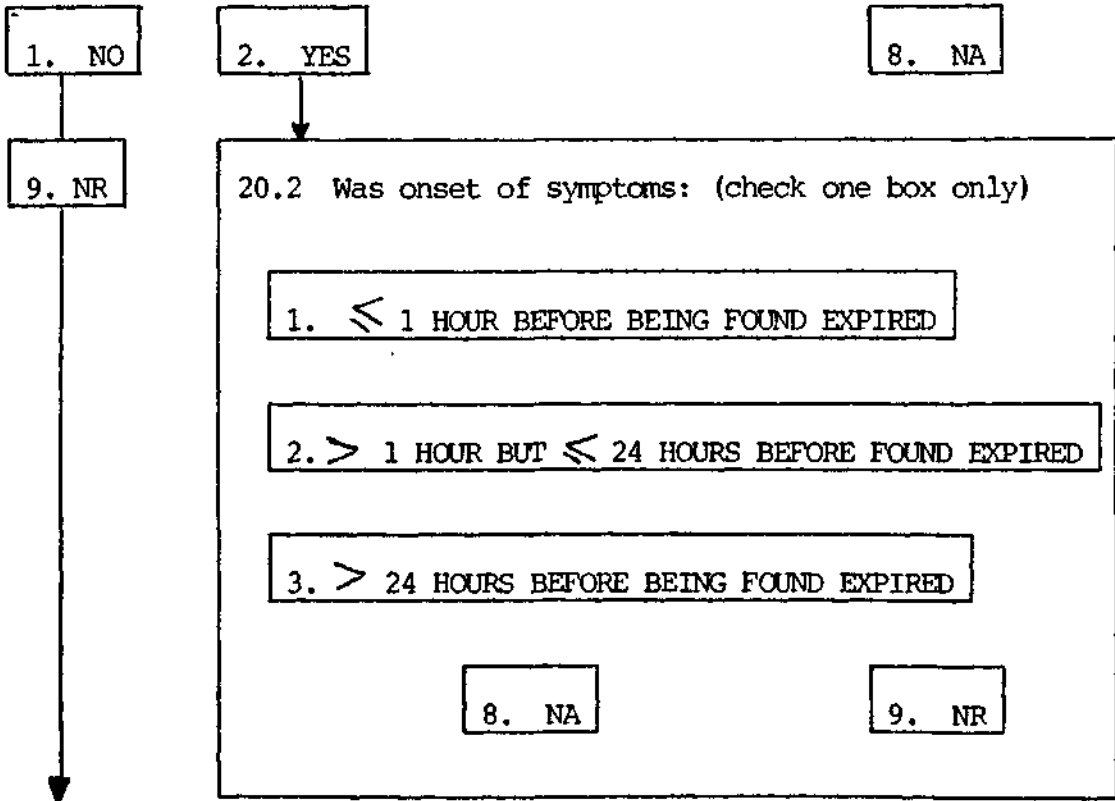
19.

FOR THOSE PATIENTS DYING DURING ADMISSION, COMPLETE Q. 20-22 OTHERWISE SKIP TO Q. 23

20. Time patient last observed before found expired or before resuscitation attempted.



20.1 Did patient have ANY of the following cardiac symptoms: fainting, dyspnea, diaphoresis, nausea/vomiting, cyanosis, and/or pain, discomfort or heaviness in the chest, neck or arms?



21. Date patient (found) expired: MONTH DAY YEAR

 NA = 8 8 8 8 8 8

HOUR

MINUTES

22. Time patient (found) expired:

NA =

--	--

8 8

--	--

8 8

1. AM

2. PM

8. NA

23.

COPY AND ATTACH ALL ECG'S AS INSTRUCTED

INFORMANT INTERVIEW ALGORITHM

- I. If Q. 10A OR 11 is answered 2 (YES), AND 1 (NO) or 9 (DK) to 10B, E, F, and H, and 1 (NO) or 9 (DK) to 22 or, if yes to 22, 2 (YES) to 22.1. AND Q. 26 is answered 1 AND Q. 29-38 are answered 1 (NO) then DSCD.
- II. If Q. 29.1 or 30.1, or 31.1 is answered 6 or 7, AND 1 (NO) to 10B, E, F, and H, and 1 (NO) to 22 or, if yes to 22, 2 (YES) to 22.1. then DSCD.
- III. If Q. 32.1 is answered 6, or 7 AND 1 (NO) or 9 (DK) to 10B, E, F and H, and 1 (NO) or 9 (DK) to 22 or, if yes to 22, 2 (YES) to 22.1. then DSCD.
- IV. If Q. 34.1 is answered 6, or 7 AND 1 (NO) or 9 (DK) to 10B, E, F and H, and 1 (NO) OR 9 (DK) to 22 or, if yes to 22, 2 (YES) to 22.1. and NO STROKE then DSCD.
- V. If Q. 26 is answered 1, AND 1 (NO) or 9 (DK) to Q. 10B, E, F and H, and 1 (NO) or 9 (DK) to 22 or, if yes to 22, 2 (YES) to 22.1. DSCD.
- VI. If Q. 29.1 or 30.1 is answered 5, 6, or 7 AND 1 (NO) or 9 (DK) to 10B, E, F and H and 1 (NO) or 9 (DK) to 22 or, if yes to 22, 2 (YES) to 22.1. then DFCHD.
- VII. If Q. 10A is answered 2 (YES) OR Q. 11 OR Q. 13 is answered 2 (YES), AND 1 (NO) or 9 (DK) to Q. 10B, E, F, and H and 1 (NO) or 9 (DK) to 22 or, if yes to 22, 2 (YES) to 22.1 then DFCHD.
- VIII. If Q. 26 is answered 2 AND 1 (NO) or 9 (DK) to 10B, E, F, and H and 1 (NO) or 9 (DK) to 22 or, if yes to 22, 2 (YES) to 22.1. then DFCHD.
- IX. If Q. 29 OR 30 is answered 2 (YES) AND 1 (NO) or 9 (DK) to 10B, E, F, and H and 1 (NO) or 9 (DK) to 22 or, if yes to 22, 2 (YES) to 22.1. then DFCHD.
- X. If Q. 29.1 OR 30.1 is answered 1, 2, 3, or 4 AND 1 (NO) or 9 (DK) to 10B, E, F, and H and 1 (NO) or 9 (DK) to 22 or, if yes to 22, 2 (YES) to 22.1. then DFCHD.
- XI. If Q. 31.1 OR Q. 32.1 is answered 1-5 AND 1 (NO) or 9 (DK) to 10B, E, F, and H and 1 (NO) or 9 (DK) to 22 or, if yes to 22, 2 (YES) to 22.1. then DFCHD.
- XII. If Q. 34.1 is answered 6 or 7 PLUS 1 (NO) or 9 (DK) to 10B, E, F and H and 1 (NO) or 9 (DK) to 22 or, if yes to 22, 2 (YES) to 22.1. and NO STROKE, then DFCHD.
- XIII. If Q. 27 is answered 1 AND 1 (NO) or 9 (DK) to 10B, E, F, and H, and 1 (NO) or 9 (DK) to 22, or if yes to 22, 2 (YES) to 22.1, then DFCHD.
- XIV. If death certificate ICD-9 Codes are 410-414 AND not DSCD or DFCHD AND Q. 10B, E, F and H are answered 1 (NO) or 9 (DK) and 1 (NO) or 9 (DK) to 22 or, if yes to 22, 2 (YES) to 22.1. then DFCHD.

- XV. If Q. 11 is answered 1 (NO) AND Q. 13 is answered 1 (NO) OR 2 (YES) to Q. 21 OR 1 (NO) to 30.1, AND 2 (YES) to 10B, E, F, or H or 2 (YES) to 22.1: then NCE.

FATAL STROKE ALGORITHM

- XVI. If Question 21 is YES (2), OR Question 22.1 is 2 (YES) OR Question 23 is YES (2), AND ICD-9 Code is not 430-437, NAS.
- XVII. If Question 21 is 1 (NO), OR Question 22.1 is 2 (YES) OR Question 23 is YES (2), AND ICD-9 Code is 430-437, PFS.
- XVIII. If Question 41.1 is YES (2), OR Question 42 is YES (2), OR Question 43 is YES (2), OR Question 44 is YES (2), and 1 (NO) or 9 (DK) to 10 B, E, F AND H AND 1 (NO) or 9 (DK) to 22 OR, if yes to 22, 2 (YES) to 22.1. FS.
- XIX. If Question 45 is YES (2), AND Question 24 is YES (2), AND ICD-9 Code is 430-437, PFS.
- XX. If Question 41.1, 42, 43, AND 44 AND both 45 AND 24 are NO (1), NAS.

Priority of Diagnoses Informant Interview Algorithm

- 1) Definite Sudden Death due to Coronary Heart Disease (DSCD)
- 2) Definite Fatal CHD (DFCHD)
- 3) Fatal Stroke (FS)
- 4) Possible Fatal CHD (PFCHD)
- 5) Possible Fatal Stroke (PFS)
- 6) Non-Cardiac Event (NCE)
- 7) No Ascertainable Stroke
- 8) No Ascertainable Event



Surveillance

Version 10
11/10/86

INFORMANT INTERVIEW SCREENER

Death Certificate # _____
Decedent's Name _____
Residence _____
Date of Death _____
Study ID _____

Informant Name _____
Address _____

Telephone _____
Relationship to Deceased _____

1. Are you familiar with _____'s medical history in the year prior to death?

1.NO

2. YES - Continue to Informant Interview - I

1.1 Is there someone I could talk to concerning _____'s medical history?

OBTAIN NAME _____
ADDRESS _____

Phone _____
Relationship to Deceased _____

2. Are you familiar with the events at the time of _____'s death?

1.NO

2. YES - Continue to Informant Interview - II

2.1 Do you know of someone I could talk to regarding the exact circumstances of _____'s death?

OBTAIN NAME _____
ADDRESS _____

Phone _____
Relationship to Deceased _____

RELIABILITY OF INFORMANT

	NO	YES	
Medical History			
3.a Did the respondent frequently contradict (himself/herself) or give information that he/she would have no way of knowing?	1 <input type="checkbox"/>	2 <input type="checkbox"/>	—
b Did the respondent seem to be reluctant to answer questions and thus might not have given all the information the interviewer would wish to know?	1 <input type="checkbox"/>	2 <input type="checkbox"/>	—
Signs and Symptoms			
4.a Did the respondent frequently contradict (himself/herself) or give information that he/she would have no way of knowing?	1 <input type="checkbox"/>	2 <input type="checkbox"/>	—
b Did the respondent seem to be reluctant to answer questions and thus might not have given all the information the interviewer would wish to know?	1 <input type="checkbox"/>	2 <input type="checkbox"/>	—
5. On the basis of these questions, give your rating of reliability of the interview.			
I. - Medical History			
1 <input type="checkbox"/> GOOD	2 <input type="checkbox"/> FAIR	3 <input type="checkbox"/> POOR	—
II. - Signs and Symptoms			
1 <input type="checkbox"/> GOOD	2 <input type="checkbox"/> FAIR	3 <input type="checkbox"/> POOR	—
6.		<input type="checkbox"/>	—
INTERVIEWER'S NAME		ID CODE	

FINAL DISPOSITION

I - Medical History

01. Interview completed with Primary Informant
02. Interview completed with Referral Informant
03. Refusal by Informant
04. Refusal by Referral
05. Not Complete - Unable to Locate Primary Informant
06. Not Complete - Unable to Locate Referral

— —

II - Signs and Symptoms

01. Interview completed with Primary Informant
02. Interview completed with Referral Informant
03. Refusal by Informant
04. Refusal by Referral
05. Not Complete - Unable to Locate Primary Informant
06. Not Complete - Unable to Locate Referral

— —

CALL RECORD

Call No.	Date	Day of Week	Time Start	Time Stop	Length of call (Mins)	Notes
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						

Introduction Letter Sent

MO

DA

YR

Permission Form Sent

MO

DA

YR

Permission Form Rec'd

MO

DA

YR

Number of Last Call

Date of Last Call

Year

Month

Day

Day of Week

M	T	W	T	F	S	S
1	2	3	4	5	6	7

Interviewer ID:

Total Length of Calls

Quality Controller ID:



Surveillance

Version 10
12/30/86

INFORMANT INTERVIEW - I

MEDICAL HISTORY

Informant Name _____

Relationship to _____
Deceased

Interview Conducted in: 1. English
2. Portuguese
3. Spanish

Type of Informant:

A. Primary - from
Death Certificate

B. Referral

List Other Sources Provided

Physician Name _____

Address _____

Physician Name _____

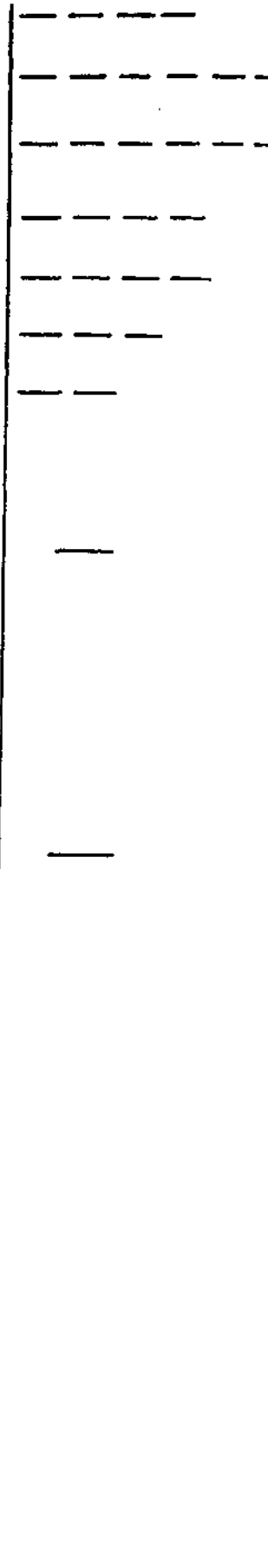
Address _____

Hospital Name _____

Address _____

Hospital Name _____

Address _____



OBTAIN RELATIONSHIP TO DECEASED

7. Was (he/she) confined to bed at any time within two weeks before death (that is, had to spend more than half of (his/her) waking hours in bed)?

1 NO

2 YES →

9 DK

8. How long had (he/she) been confined to bed?

1 < 2 DAYS

5 < 6 WKS

2 < 1 WK

6 ≥ 6 WKS

3 < 2 WKS

8 NA

4 < 4 WKS

9 DK

9. Was _____ a resident of a nursing home at the time he/she died?

1 NO

2 YES →

9 DK

Name of nursing home
Address/Telephone

10. In the year before _____'s death, did a doctor ever say that (he/she) had the following; or did the doctor treat (him/her) for any of these conditions; or prescribe any of these medications?

	NO	YES	DK
A. angina pectoris, heart pains, or was he/she taking nitroglycerin?.....	1 <input type="checkbox"/>	2 <input type="checkbox"/>	9 <input type="checkbox"/>
B. abdominal aneurysm, bulging or leaking of the aorta?.....	1 <input type="checkbox"/>	2 <input type="checkbox"/>	9 <input type="checkbox"/>
C. congestive heart failure, fluid in/on lungs, or was he/she taking lanoxin, digoxin, or digitalis?.....	1 <input type="checkbox"/>	2 <input type="checkbox"/>	9 <input type="checkbox"/>
D. high blood pressure?.....	1 <input type="checkbox"/>	2 <input type="checkbox"/>	9 <input type="checkbox"/>
E. severe breathing problems from emphysema or chronic lung disease?.....	1 <input type="checkbox"/>	2 <input type="checkbox"/>	9 <input type="checkbox"/>
F. cirrhosis of the liver or liver failure?.....	1 <input type="checkbox"/>	2 <input type="checkbox"/>	9 <input type="checkbox"/>

- | | NO | YES | DK |
|---|----------------------------|----------------------------|----------------------------|
| G. diabetes?..... | 1 <input type="checkbox"/> | 2 <input type="checkbox"/> | 9 <input type="checkbox"/> |
| H. kidney failure requiring dialysis or kidney machine?..... | 1 <input type="checkbox"/> | 2 <input type="checkbox"/> | 9 <input type="checkbox"/> |
| I. weakness of heart muscle, sometimes called myocarditis or cardiomyopathy?..... | 1 <input type="checkbox"/> | 2 <input type="checkbox"/> | 9 <input type="checkbox"/> |
| J. rheumatic fever or rheumatic heart disease?..... | 1 <input type="checkbox"/> | 2 <input type="checkbox"/> | 9 <input type="checkbox"/> |
| K. mitral valve prolapse, floppy heart valve, or a clicking heart valve?..... | 1 <input type="checkbox"/> | 2 <input type="checkbox"/> | 9 <input type="checkbox"/> |
| L. Other heart-related problems.....
specify _____ | 1 <input type="checkbox"/> | 2 <input type="checkbox"/> | 9 <input type="checkbox"/> |

11. At anytime, did _____ ever have a heart attack for which (he/she) was in the hospital for a week or more?

1 NO 2 YES 9 DK

↓

11.1 Was that within the 4 weeks before he/she died?

1 NO 2 YES 8 NA 9 DK

12. At anytime, did _____ ever have a stroke for which (he/she) was in the hospital for 2 days or more?

1 NO 2 YES 9 DK

13. Did _____ have coronary artery or heart surgery at any time within the 4 weeks before death?

1 NO

2 YES →

9 DK

13.1 At any time after surgery, was (he/she) able to resume (his/her) usual level of daily activities?

1 NO

2 YES

8 NA

9 DK

14. In the year before _____ 's death, was (he/she)
in the hospital for any reason and then discharged from the hospital?

1 NO
↓
GO TO
Q. 20

2 YES
↳

15. Within that last year, how many times was he/she
hospitalized?

88 NA 99 DK

LIST MOST RECENT VISIT FIRST

16. What hospital was he/she in?

Name of hospital _____

City _____

When was he/she discharged?

Date
 MO DY YR

9 DK
↓
GO TO
Q. 20

17. What hospital was he/she in before that?

Name of hospital _____

City _____

When was he/she discharged?

Date
 MO DY YR

18. What hospital was he/she in before that?

Name of hospital _____

City _____

When was he/she discharged?

Date
 MO DY YR

19. What hospital was he/she in before that?

Name of hospital _____

City _____

When was he/she discharged?

Date
 MO DY YR

20. Did _____ have a regular physician? (PHYSICIAN WITH THE MOST INFORMATION)

1 NO 2 YES 9 DK

NO → GO TO Q. 20.2

YES ↓

DK → GO TO Q. 20.2

Physician's name: _____

Practice/Clinic: _____

Address/Telephone: _____

20.1. Did (he/she) see (his/her) regular physician within one year before death?

1 NO 2 YES 8 NA 9 DK

20.2 Did (he/she) see any other physician within one year before death?

1 NO 2 YES 8 NA 9 DK

Physician's name: _____

Practice/Clinic: _____

Address/Telephone: _____

21. Had he/she ever had surgery for a bad heart valve?

1 NO 2 YES 8 NA 9 DK

22. Did he/she have cancer during the year prior to death?

1 NO 2 YES 8 NA 9 DK

22.1. Was it skin cancer?

1 NO 2 YES 8 NA 9 DK

23. Did he/she have an injury to the head in the two days prior to death that knocked him/her out?

1 NO 2 YES 8 NA 9 DK

24. Was he/she ever diagnosed as having high blood pressure?

1 NO 2 YES 8 NA 9 DK

25.A I would like permission to review some of the medical records. IF INFORMANT IS NEXT-OF-KIN, PROCEED. IF NOT, SKIP TO Q 25.B May I have your consent to obtain further information from the hospital/physician/both?

1 NO

2 YES → I will send you a permission form(s) to sign and mail back to me in an envelope that I'll enclose. You should receive it within a few days.

(SKIP 25.B)

VERIFY ADDRESS _____

8 NA

25.B May I have the name, address and phone number of a family member to contact for consent to obtain further information from the hospital/physician/both?

1 NO

2 YES → NAME _____
ADDRESS _____
PHONE _____

8 NA

RETURN TO SCREENER Q.2

NEUROBEHAVIORAL
TESTING PROTOCOL

3. NEUROPSYCH OVERVIEW

-2-

Introduction

The neuropsychological functioning of study participants was derived from a battery of tests selected to assess the specific mental abilities hypothesized to be impaired in subjects with Agent Orange exposure or subjects with significant combat exposure in Vietnam. Neuropsychological tests were used due to their objective scoring, standardized administration procedures, and their sensitivity for assessing problems in the areas of memory, attention, dexterity, language, visual-spatial, and higher level mental functions. These test scores were used as a means for group comparisons rather than as absolute measures of these ability areas. All of these tests do measure multiple abilities (multifactorial) which can influence a subject's final score.

ALL TEXT REFERENCES ARE FROM LEZAK

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MURIEL DEUTSCH LEZAK

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Neuropsychological Testing Interim Analysis

Medical Examination Component Vietnam Experience Study

I. A Priori Hypotheses

A. Neuropsychological/Psychological Effects of Agent Orange or Dioxin:

1. Decreased memory system functioning
2. Decreased mental control and/or attention
3. Decreased dexterity
4. Decreased arousal/activation system functioning
5. Decreased frontal/executive system functioning
6. Increased levels of anxiety, depression, somatization
7. Increased emotional lability

B. Neuropsychological/Psychological Effects Related to Military Service in Vietnam:

1. Increased levels of PTSD and/or PTSD related symptoms
2. Increased levels of anxiety, depression, somatization
3. Increased alcohol and/or drug abuse
4. Increased psychopathology (general)
5. Decreased mental control, attention, or memory

The above hypotheses are based on the literature review provided in Appendix C.

4. WRAT - R READING SUBTEST

~~A/D~~ WRAT-R Reading Subtest Grade Equivalent Score: The reading subtest from the Wide Range Achievement Test-Revised consists of reading of single words and is highly correlated with educational background.

THE WIDE RANGE ACHIEVEMENT TEST (WRAT) (Jastak and Jastak, 1965)

This battery format instrument earns its "wide range" title by its applicability from early childhood through the middle adult years. It tests three academic skills—spelling, reading, and arithmetic—each at two age ranges or "Levels." The Level I age range is from five through 11; Level II covers ages 12 to "45-0 and over."

The Level I Spelling test comes in three parts: copying a short set of nonsense figures and writing one's name are tasks only at Level I; a dictation task differs from the Level II Spelling test in word difficulty. Both Arithmetic levels have two parts, an orally administered section for the lowest achievement levels, and a written arithmetic test. Ten minutes are allowed for written arithmetic at both levels. Reading begins with letter reading and recognition at Level I and continues with a 75-word reading and pronunciation list. At Level II, Reading involves only the word list.

This test is carefully standardized with a full set of norms for each subtest. Level I has age norms for each half-yearly interval between ages 5 and 12. Level II age norms continue at half-yearly intervals from 12 to 16; from 16 to 20, they span two-year intervals, and from 20 to 45 they cover five-year intervals. All raw scores can be converted to school grades, standard scores, or percentiles. Thus, this is a flexible test, adaptable for inclusion in any set of tests.

The standard deviation of the WRAT is only 10 (see p. 145). With a mean set at 100, an examiner familiar with the scoring systems of the Wechsler or Stanford-Binet scales may misinterpret the WRAT scores if the smaller standard deviation is not taken into account.

All three WRAT subtests are heavily weighted with the general ability factor, and the verbal factor contributes a large component to Reading and Spelling. Arithmetic has little of the verbal factor, but a "motivation" factor is involved.

The WRAT Arithmetic subtest tests the ability to perform written arithmetic. A feature of the WRAT Arithmetic test that is valuable for neuropsychological assessment is the variety of mathematical problems it poses. These include application of the four basic arithmetic operations to two- and three-digit numbers, to decimals, percentages, fractions, and to algebraic problems, as well as the translation of Roman numerals, weights, and measures. Problems concerning squares, roots, and some geometric constructs are also presented. Thus, when a patient's mathematical performance is defective, the examiner can determine by inspection of his worksheet whether his difficulties are due to a dyscalculia of the spatial type, a symbol or number alexia, or an anarithmetria in which number concepts or basic operations have been lost. The lower level arithmetic problems can be given when the patient is unable to do enough at the adult level for a fair sampling of his arithmetic skills.

The Arithmetic subtest does have some drawbacks when used for neuropsychological purposes. Many brain damaged patients are unable to answer more than a few items within the allotted ten minutes. To evaluate a performance on the basis of the test norms, which take time into account, the examiner need only note how much of the test the patient completed at ten minutes, without disturbing the patient. Stopping the patient before he has finished may greatly restrict the amount of information that can be obtained about his ability to do arithmetic and the nature of any disability he

may have in this area. The small print and scant space surrounding each problem can create some difficulty, particularly for older patients and patients with visual acuity problems. A larger scale version of this test, allowing for more computation space around each problem, would solve this difficulty and make it easier for the examiner to follow the patient's computational efforts. The standard score and percentile norms reflect a performance decline from ages 25 to 50, but they do not take into account differences at older age levels.

Children's Tests

Patients with severe intellectual handicaps may give so few scorable responses to some or all of the WAIS subtests that the examiner has little opportunity to assess their capabilities or the relative strengths and weaknesses of different functions. Children's or infant's tests may enable them to display a broader range of their behavior than and preschool levels but lacks the advantages of battery tests. Four of the best known children's tests—the Wechsler Intelligence Scale for Children, The Wechsler Preschool and Primary Test of Intelligence, the Pictorial Test of Intelligence, and the Illinois Test of Psycholinguistic Abilities—are in battery form. A fifth, the Leiter, is a nonverbal counterpart of the Binet intended for use with patients who have speech and hearing handicaps.

THE WECHSLER INTELLIGENCE SCALE FOR CHILDREN (WISC and WISC-R) (Wechsler, 1949, 1974)

The WISC covers the age range from 5 to 15 years 11 months, and the age range of its revision, the WISC-R, is 6 years to 16 years 11 months. They contain the same subtests as the WAIS in an almost identical format, but all of the subtests except Digit Span begin with considerably simpler items. Although most WISC and WISC-R items are the same, outmoded WISC items have been dropped from the WISC-R, and some of the new WISC-R picture items have black or female subjects. The WISC-R blocks conform to the two-color (red and white) WAIS blocks, replacing the four-color WISC blocks. The number sequences of the WISC and WISC-R Digit Span subtest are the same length and difficulty as those of the WAIS. There is an alternate form of Digit Symbol (called Coding on the WISC) for children under nine on the WISC, under eight on the WISC-R, and suspected mental defectives. Coding uses five geometric symbols (star, circle, etc.) instead of numbers, and the symbols to be written in are simpler than those of the more difficult WISC version of the WAIS. Administration instructions are similar, and for many subtests, identical, to those of the WAIS.

Standard score equivalents of WISC and WISC-R subtest raw scores are given for each four-month interval covered by the scale. However, in interpreting WISC and WISC-R scores for adult patients, the examiner should use the Table of Test Age Equivalents (p. 113 of the WISC Manual, p. 189 of the WISC-R Manual), which will give the age equivalents of the patient's score on any of the WISC subtests.

The WISC contains a maze test that has no WAIS counterpart. It consists of printed mazes (eight on the WISC, nine on the WISC-R) of varying sizes and complexity, which are given in order of difficulty. Scoring is based on the number of errors; there

WIDE RANGE ACHIEVEMENT TEST - REVISED LEVEL 2

Page 4

Reading, Level 2

Two letters in name (2)

A B O S E R T H P I U Z Q

milk city in tree animal himself between chin split

form grunt stretch theory contagious grieve toughen aboard

triumph contemporary escape eliminate tranquillity conspiracy

image ethics deny rancid humiliate bibliography unanimous

predatory alcove scald mosaic municipal decisive contemptuous

deteriorate stratagem benign desolate protuberance prevalence

regime irascible peculiarity pugilist enigmatic predilection

covetousness soliloquize longevity abysmal ingratiating oligarchy

coercion vehemence sepulcher emaciated evanescence centrifugal

subtlety beatify succinct regicidal schism ebullience misogyny

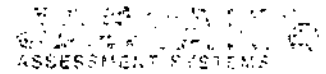
beneficent desuetude egregious heinous internecine synecdoche

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WRAT-R²

Raw Score to Grade Equivalents



RS	READING	35 40 45 50 55 60																				
	1-30																			65-89		
GE	Below 3	3B	3E	4B	4E	5B	5E	6B	6E	7B	7E	8B	8E	9B	9E	10B	10E	11B	11E	12B	12E	Above 12

SEM = 2

RS	SPELLING	15 20 25 30 35																				
	1-10																			36-51		
GE	Below 3	3B	3E	4B	4E	5B	5E	6B	6E	7B	7E	8B	8E	9B	9E	10B	10E	11B	11E	12B	12E	Above 12

SEM = 2

RS	ARITHMETIC	15 20 25 30 35																				
	1-14																			40-66		
GE	Below 3	3B	3E	4B	4E	5B	5E	6B	6E	7B	7E	8B	8E	9B	9E	10B	10E	11B	11E	12B	12E	Above 12

SEM = 2

U. WAIS-R

② WAIS-R Information Subtest Scale Score: The information subtest from the WAIS-R is a measure of general information which is highly correlated with educational and socioeconomic background. It has also been considered as a measure of long-term memory as most of the questions require the subject to recall information typically learned in school. This test is also correlated with general IQ and verbal abilities.

② WAIS-R Block Design Subtest Scale Score: The block design subtest from the WAIS-R is a measure of visual-perceptual-motor, visual-spatial, and non-verbal reasoning abilities. This test also is correlated with general IQ and is timed so that mental and motor speed are a component of a subject's performance.

sitive to memory defect, distractibility, and motor slowing, whereas these problems are not characteristic of people who are simply dull and not organically impaired. The concrete thinking of brain damage is distinguishable from that of psychiatric conditions in that the former tends to occur consistently, or at least regardless of the emotional meaningfulness of the stimulus, whereas the latter is more apt to vary with the emotional impact of the stimulus on the patient or with any number of factors external to the examination. Concrete thinking alone is not indicative of brain damage in patients of normally low intellectual endowment or in long-term chronic psychiatric patients. A concrete approach to problem solving, which shows up in a relatively depressed Similarities score, with perhaps some lowering of Comprehension, Block Design, or Picture Completion scores, may be the most pronounced residual intellectual defect of a bright person who has had a mild brain injury. However, patients with lesions primarily involving prefrontal structures may be quite impaired in their capacity to handle abstractions or to take the abstract attitude and yet not show pronounced deficits on the close-ended, well-structured Wechsler test questions (see pp. 78-79, 82).

Other than a few fairly distinctive but not mutually exclusive patterns of lateralized and diffuse damage, the Wechsler-based evaluation of whether brain damage is present depends on whether the subtest score pattern makes neuropsychological sense. For instance, the widespread tissue swelling that often accompanies a fresh head injury or rapidly expanding tumor results in confusion, general dulling, and significant impairment of memory and concentration functions that appear on the WAIS batteries as significantly lowered scores on almost all subtests, except perhaps time-independent verbal tests of old, well-established speech and thought patterns (Conen and Brown, 1968). Bilateral lesions generally produce changes in both verbal and visuospatial functions and involve aspects of memory and attention as well.

Evaluation of *organicity* by pattern analysis requires knowledge of what is neuropsychologically possible and an understanding of the patient's behavioral capabilities as demonstrated on a WAIS battery and other measures of mental functions that have been examined within the context of the patient's life experiences, current psychosocial situation, and the medical history. Pattern analysis applies best to patients with recent or ongoing brain changes and is less effective in identifying organic disorders in psychiatrically disturbed patients. The Wechsler subtest score patterns of patients with old, static brain injuries, particularly those who have been institutionalized for a long time, tend to be indistinguishable from those of chronic institutionalized psychiatric patients and is less effective in identifying organic disorders in psychiatrically disturbed patients (see pp. 233-234).

The Wechsler Intelligence Scales Subtests

The standard examination procedure calls for the administration of the 11 subtests of the Wechsler scales in the order of their presentation below. When all 11 tests are given, testing time generally runs from one and one quarter to two hours. The WAIS

and WAIS-R Manuals give the standard administration instructions in detail (D. Wechsler, 1955, 1981).

In the interests of maintaining a standardized administration, the examiner should not attempt to memorize the questions but rather should read them from the manual. When questions have been memorized, the examiner is liable to insert a word here or change one there from time to time without being aware of these little changes. Ultimately they add up so that the examiner may be asking questions that differ not only in a word or two but in their meaning as well. I have found that the only way to guard against this very natural tendency is to use the manual for every administration.

Administration of the 11 subtests need not follow the standard order of presentation (see p. 114). Rather, the examiner may wish to vary the subtest order to meet the patient's needs and limitations. Patients who fatigue easily can be given more taxing subtests, such as Arithmetic or Digit Span, early in the testing session. If the patient is very anxious about the tests, the examiner will want him first to take tests on which he is most likely to succeed before he tackles more difficult material.

Edith Kaplan recommends alternating Verbal and Performance Scale subtests of the WAIS so that patients who may have predominantly verbal or predominantly visuospatial deficits are not faced with a series of failures but rather can enjoy some successes throughout the examination. I have found this presentation pattern very helpful in preventing buildup of tension or discouragement in these patients. Alternating between the school-like question-and-answer items of the Verbal Scale subtests and the puzzle-and-games Performance Scale items also affords a change in pace that keeps the interest of patients whose insight, motivation, or capacity to cooperate is impaired better than does presentation in the originally prescribed order. The WAIS-R incorporates these advantages in a recommended order of administration that alternates Verbal Scale and Performance Scale subtests.

The examiner also need not complete all subtests in one sitting but can stop whenever he or his patient becomes restless or fatigued. In most instances, the examiner calls the recess at the end of a subtest and resumes testing at some later time. Occasionally, a patient's energy or interest will give out in the middle of a subtest. For most subtests, this creates no problem; the test can be resumed where it had been stopped. However, the easy items on Similarities, Block Design, and Picture Arrangement provide some people the practice they need to succeed at more difficult items. If the examination must be stopped in the middle of any of these three tests, the first few items should be repeated at the next session so the patient can reestablish the set necessary to pass the harder items.

Savage and his colleagues (1973) found that people over the age of 70 tended to be uncomfortably sensitive to failures. Negative reactions were likely to show up when the examiner was following the requirement that subtests be continued for a given number of failures. Since many older people enjoyed doing "puzzles," they tolerated failure better on Performance Scale than on Verbal Scale subtests. When faced with the choice of giving the required number of items or discontinuing early to reduce the elderly patient's discomfort, I usually discontinue. In most cases, even if the

patient succeeded on one or two of the more difficult items, continuation would not make a significant difference in the score. When the patient appears to be capable of performing at a higher level than he seems willing to attempt and it is important to document this information, the omitted items can be given at a later time, after the patient has had some obvious successes or when he seems more relaxed.

A verbatim record of the patient's answers and comments makes this important dimension of his test behavior available for leisurely review. The examiner who has learned shorthand has a great advantage in this respect. Slow writers in particular might benefit from an acquaintance with brief-hand or speedwriting.

Many examiners routinely use only nine or ten of the eleven WAIS battery subtests (McFie, 1975; A. Smith, 1966b). Most of my examinations do not include Vocabulary because the information it adds is redundant when the other verbal subtests have been given. It also takes the longest of any of the verbal subtests to administer and score. In my examinations a vocabulary test is usually included in the paper and pencil battery or a picture vocabulary test is substituted for patients unable to read or write. Sometimes I exclude Digit Symbol and give the Symbol Digit Modalities Test instead (when I want to compare auditory and graphic response speed on the symbol substitution task and also look for tendencies toward spatial rotation or disorientation, I may give them both). When a symbol substitution test is given to patients with pronounced motor disability or motor slowing who will obviously perform poorly on this highly time-dependent test, their low scores add no new information, making this test redundant, too.

When there are time pressures, the examiner may wish to use a "short form" of the WAIS battery, that is, a set of only three, four, or five subtests selected to give a reasonably representative picture of the patient's functioning (Duke, 1967). Short forms were originally developed to produce a quick estimate of the Full Scale IQ score. Since estimation of an aggregate IQ score is not the goal of the neuropsychological examination, selection of subtests for brief neuropsychological screening need not be made on the basis of how well the combined score from the small set of tests approximates the Full Scale score. So long as the subtests are handled as discrete tests in their own right, the examiner can include or exclude them to suit his patient's needs and abilities and the requirements of the examination.

"Split-half" administrations, in which only every other item is given, also save time but may lose accuracy. One study (Zytowski and Hudson 1965) found that with the exception of Vocabulary, the validity coefficients of split-half scores correlated with whole subtest scores range below .90; and of the Performance Scale subtests, only Block Design is above .80. Satz and Mogel (1962) devised an abbreviated set of scales that includes all the WAIS scales. It uses mostly split-half (odd items only) administrations excepting on Information, Vocabulary, and Picture Completion in which every third item is given. Digit Span and Digit Symbol administrations remain unchanged. The authors report that only Information ($r = .89$), Comprehension ($r = .85$), Block Design ($r = .84$), and Object Assembly ($r = .79$) have correlations below .90 with the whole subtests. G. C. Marsh (1973) obtained fairly comparable correlations on a cross-validation study of the Satz-Mogel format and concluded that

this format "is an adequate substitute for the long-form WAIS when it is used as a test of general intelligence with neurology or psychiatry patients." She found, however, that with the abbreviated forms of Information, Comprehension, Picture Completion, and Picture Arrangement, 15-20% of the scores of the group of neurology patients and 18-30% of the scores of the psychiatry patients showed a deviation of three or more scaled scores from their whole subtest performances. Marsh cautioned against using this format when doing pattern analysis. Goebel and Satz (1975) examined the relationship between subtest scaled score profiles obtained on the Satz-Mogel abbreviation of the WAIS and profiles derived in the standard administration, using multivariate procedures. Their data suggest that the abbreviated format does generate subtest profiles that can be used with relative confidence when comparing an individual profile with a set of statistically derived clinical profile types. These findings, though, apply only to the classification of overall profiles, and do not answer the questions raised by Marsh's study regarding the clinical use of abbreviated scale scores when doing inductive pattern analysis.

Neuropsychologically useful information can be gained by incorporating the face-sheet identification and personal information questions into the examination proper. These questions give the examiner the opportunity of evaluating the patient's orientation in a very naturalistic—and thus quite inoffensive—manner and also of ensuring that the important employment and education data have been obtained. ("Race" or "color" is usually obvious.) Only the examiner who routinely asks patients about the date, their age and date of birth, and similar kinds of information usually taken for granted, can appreciate how often neurologically impaired patients fail to answer these questions reliably and how important it is to know this when evaluating and planning for a patient. I also always make a point of filling in my name along with the rest of the information requested at the top of the page and repeating it while I write as many patients, particularly in a large medical center where they may be examined by many people, may not remember the examiner's name and may be too embarrassed to ask.

Many of the subtests present administration or scoring problems peculiar to that subtest. These will be noted in the discussion of each subtest below.

Verbal Scale Subtests

INFORMATION

The Information items test general knowledge normally available to persons growing up in the United States. WAIS battery forms for other countries contain suitable substitutions for items asking for peculiarly American information. The items are arranged in order of difficulty from the four simplest, which all but severely retarded or organically impaired persons answer correctly, to the most difficult, which only few adults pass. The relative difficulty level of some of the WAIS items has probably changed over the years, particularly for the younger age groups. The recent ramblings of the date for celebrating Washington's birthday from year to year (see p.

241), the almost universal (in the United States) inclusion of the *Odyssey* or the *Iliad* in the high school curriculum, and the increased popular interest in Islamic culture will necessarily be reflected in differences in the proportion of persons within and between the different age groups who can answer these questions correctly. In addition, increases in the level of education in the United States, particularly in the older age groups, may have raised the population mean score on the Information subtest. Certainly my clinical experience suggests that this is the case.

I make some additions to Wechsler's instructions. When a patient taking the WAIS gives a very low or very high estimate of the height of the average American woman, I usually ask, as if it were the next question in the test, "What does *average* mean?" to determine whether the response represents an estimation error (see pp. 501-502) or ignorance of the concept of average. I spell "Koran" after saying it since it is a word people are more likely to have read than heard, and if heard, may have been pronounced differently. When patients who have not gone to college answer any of the items from 21 to 25 correctly so that they will be given one or more of the last four items, I usually make some comment such as, "You have done so well that I have to give you some questions that only a very few, usually college-educated, people can answer," thus protecting them as much as possible from unwarranted feelings of failure or stupidity if they are unfamiliar with the items' topics. When a patient gives more than one answer to a question and one of them is correct, the examiner must insist on the patient telling which answer he prefers to be scored as it is not possible to score a response containing both right and wrong answers. I usually ask patients to "vote for one or another of the answers."

Although the standard instructions call for discontinuation of the test after five failures, the examiner may use discretion in following this rule, particularly with brain injured patients. On the one hand, some neurologically impaired patients with prior *average* or higher intellectual achievements are unable to recall once-learned information on demand and therefore fail several simple items in succession. When such patients give no indication of being able to do better on the increasingly difficult items and are also distressed by their failures, the examiner loses little by discontinuing this task early. If he has any doubts about the patient's inability to answer the remaining questions, he can give the next one or two questions later in the session after the patient has had some success on other subtests. On the other hand, bright but poorly educated subjects will often be ignorant of general knowledge but have acquired expertise in their own field which will not become evident if the test is discontinued according to rule. Some mechanics, for example, or nursing personnel, may be ignorant about literature, geography, and religion, but know the boiling point of water. When testing an alert person with specialized work experience and a limited educational background who fails five sequential items not bearing on his personal experience, I usually give all higher level items that might be work-related.

When giving the Information subtest to a patient with known or suspected organic impairment, it is very important to differentiate between failures due to ignorance, loss of once-stored information, and inability to retrieve old learning or say it on command. (See *Testing the Limits*, pp. 114-115.) Patients who cannot answer questions

at levels higher than warranted by their educational background, social and work experiences, and vocabulary and current interests have probably never known the answer. Pressing them to respond may at best waste time, at worst make them feel stupid or antagonize them. However, when patients with a high school education cannot name the capital of Italy or give the direction from Chicago to Panama, I generally ask them if they once knew the answer. Many patients who have lost information that had been in long-term storage or have lost the ability to retrieve it, usually can be fairly certain about what they once knew but have forgotten or can no longer recall readily. When this is the case, the kind of information they report having lost is usually in line with their social history. The examiner will find this useful both in evaluating the extent and nature of the patient's impairments and in appreciating his emotional reactions to his condition.

Should a patient acknowledge that he could have answered the item at one time, appear to have a retrieval problem or difficulty verbalizing the answer, or have a social history that would make it likely he once knew the answer (e.g., a Catholic who cannot identify the Vatican), then information storage can be tested by giving the patient several possible answers to see whether he can recognize the correct one. I always write out the multiple-choice answers so the patient can see all of them simultaneously and need not rely on a possibly failing auditory memory. For example, when patients who have completed high school are unable to recall *Hamlet's* author, I write out, "Longfellow (or Kipling on the WAIS-R), Tennyson, Shakespeare, Wordsworth." Occasionally a patient taking the WAIS points to "Longfellow." If there are other indications of perseverative behavior, then this response probably gives one more instance of it; certainly it raises the suspicion of perseveration since the patient had just recently heard that name. More often, the patient identifies Shakespeare correctly, thus providing information both about his fund of knowledge (which he has just demonstrated is bigger than his Information subtest score will indicate) and his retrieval problem. Nonaphasic patients who can read but still cannot identify the correct answer on a multiple-choice presentation probably do not know, cannot retrieve, or have truly forgotten the answer.

The additional information that the multiple-choice technique may communicate about the patient's fund of knowledge raises scoring problems. Since the test norms were not standardized on this kind of administration, additional score points for correct answers to the multiple-choice presentation cannot be evaluated within the same standardization framework as scores obtained according to the standardization rules. On the other hand, this valuable information should not be lost or misplaced. To solve this problem, I use *double scoring*; that is, I post both the age-graded standard score the patient achieves according to the standardization rules and, usually following it in parentheses, another age-graded standard score based on the "official" raw score plus raw score points for the items on which the patient demonstrated knowledge but could not give a spontaneous answer. This method allows the examiner to make an estimate of the patient's fund of background information based on a more representative sample of behavior, given the patient's impairments. The disparity between the

two scores can be used in making an estimate of the amount of deficit the patient has sustained, while the lower score alone indicates the patient's present level of functioning when he must retrieve verbal information without assistance.

On this and other subtests, test administration adapted to the patient's deficits with double-scoring to document performance under both standard and adapted conditions enables the examiner to discover the full extent of the neurologically impaired patient's capacity to perform the task under consideration. Effective use of this method involves both testing the limits of the patient's capacity and, of equal importance, standardized testing to ascertain a baseline against which performance under adapted conditions can be compared. In every instance, the examiner should test the limits only after giving the test item in the standard manner with sufficient encouragement and a long enough wait to satisfy any doubts about whether the patient can perform correctly under the standard instructions.

Information and Vocabulary are the best WAIS battery measures of general ability, that ubiquitous test factor that appears to be the statistical counterpart of learning capacity plus mental alertness, speed, and efficiency. Information also tests verbal skills, breadth of knowledge, and—particularly in older populations—remote memory. Information tends to reflect formal education and motivation for academic achievement (Saunders, 1960a). It is one of the few subtests in the WAIS batteries that can give spuriously high ability estimates for overachievers, or fall below the subject's general ability level because of early lack of academic opportunity or interest. Information (WAIS) contains ten items that are not equally difficult for men and women, the difference favoring men to a significant degree.

In brain injured populations, Information tends to appear among the least affected WAIS battery subtests (K. O'Brien and Lezak, 1981; Sklar, 1963). Although a slight depression of the Information score can be expected with brain injury of any kind, because performance on this subtest shows such resiliency it often can serve as the best estimate of original ability. In individual cases, a markedly low Information score suggests left hemisphere involvement, particularly if verbal tests generally tend to be relatively depressed and the patient's history provides no other kind of explanation for the low score. Thus, the Information performance can be a fairly good predictor of the hemispheric side of a suspected brain lesion (Reitan, 1955b; A. Smith, 1966b; Spreen and Benton, 1965).

COMPREHENSION

This subtest includes two kinds of open-ended questions: 11 (13 in the WAIS-R) test common-sense judgment and practical reasoning, and the other three ask for the meaning of proverbs. Comprehension items range in difficulty from a common-sense question passed by all nondefective adults to a proverb that is fully understood by fewer than 22% of adults (Matarazzo, 1972).

Since some of the items are lengthy, the examiner must make sure that patients whose immediate verbal memory span is reduced have registered all of the elements

BLOCK DESIGN

This is a construction test in which the subject is presented with red and white blocks, four or nine, depending on the item. The task is to use the blocks to construct replicas of two block constructions made by the examiner and eight (on the WAIS) or seven (WAIS-R) designs printed in smaller scale (see Fig. 9-3). The order of presentation differs from the order of difficulty. Diller and his co-workers (1974) found that, for elderly subjects, the second design had a difficulty level intermediate between WAIS designs 5 and 6. Generally speaking, at each level of complexity, the WAIS even-numbered items are likely to be more difficult than the odd-numbered items. Designs



Fig. 9-3. Block Design subtest. (Reproduced by permission of The Psychological Corporation.)

1, 3, 5, and 7 (1, 4, and 6 of the WAIS-R) are made up of distinguishable block faces, mostly plain squares; diagonals occur discretely so that when patients with visuospatial disorders or dull or careless persons fail one of these items, it is more likely to be due to incorrect orientation of the diagonal of a red-and-white block than to errors in laying out the overall pattern. In contrast, the diagonal patterns of the even-numbered designs reach across two- and three-block spans. Concrete-minded persons and patients (particularly those with right hemisphere damage) with visuospatial deficits have particular difficulty constructing these diagonal patterns. The four-block designs have one-minute time limits and the nine-block designs two-minute limits. The subject can earn one or two bonus points for speed on the last four designs of the WAIS, and speed credits are given on items 3 to 9 of the WAIS-R.

Unlike the example pictured in Figure 9-3, the designs to be copied should be placed directly in front of the patient, just back far enough to allow the patient room to work. (Also unlike the example depicted in Figure 9-3, the patient's working area should be free of distractions such as other test material, the examiner's booklet, etc.) All subjects begin with the first item, which is presented and demonstrated as a block-copying rather than a design-copying test. The first and second items can be repeated should the subject fail to produce a correct design within the time limits, and the manual allows some leeway for demonstration and explanation of these items (Wechsler, 1955, 1981). Only severely retarded or impaired adults are unable to succeed on either trial of the first two items. The third item of the WAIS is much easier than the second one and is given to all subjects, regardless of their performance on items 1 or 2. No demonstrations are allowed after the first two items. The test is normally discontinued after three failures.

The examiner may wish to vary the standard procedures to give the patient an opportunity to solve problems failed under standard conditions or to bring out different aspects of the patient's approach to the Block Design problems. As on the other timed tests, it is useful to obtain two scores if the patient fails an item because he exceeded the time limit. When the examiner times discreetly, the patient remains unaware that he has overrun his time so that if he completes the design correctly, he will have the full satisfaction of his success. Usually, permitting the patient to complete the design correctly means waiting an extra minute or half minute beyond the allotted time. With a very slow patient, the examiner has to decide whether waiting the five or seven minutes the patient takes to work at a problem is time well spent observing him or providing an opportunity for success; whether the patient's struggle to do a difficult or perhaps impossible task distresses him excessively; or whether the patient needs the extra time if he is to succeed at this kind of task at all. It is usually worthwhile to wait out a very slow patient on at least one design to see him work through a difficult problem from start to finish and to gauge his persistence. However, if the patient is obviously in over his depth and either does not appreciate this or refuses to admit defeat, the examiner needs to intervene tactfully before the task so upsets or fatigues him that he becomes reluctant to continue taking any kind of test.

Brain damaged patients sometimes do not comprehend the Block Design task when given the standard instructions alone. An accompanying verbal explanation like the

following may help clarify the demonstration: "This lower left-hand (patient's left) corner is all red, so I put an all red block here. The lower right-hand corner is also all red, so I put another all red block there. Above it in the upper right corner goes what I call a 'half-and-half' block [red and white halves divided along the diagonal]; the red runs along the top and inside so I'll put it above the right-hand red block this way (emphasizing the angulation of the diagonal)", etc. Following completion of the test the examiner can bring out any design that puzzled the patient or elicited an atypical solution and ask him to try again. The examiner can then test for the nature of the patient's difficulty by having him verbalize as he works, by breaking up the design and constructing and reconstructing it in small sections to see if simplification and practice help, or by giving the patient blocks to copy instead of the smaller sized and unlined printed design. The examiner can test the patient's perceptual accuracy alone by asking him to identify correct and incorrect block reproductions of the designs (Bortner and Birch, 1962).

Block Design lends itself well to qualitative evaluation. The manner in which the patient works at Block Design can reveal a great deal about his thinking processes, work habits, temperament, and attitudes toward himself. The ease and rapidity with which the patient relates the individual block sides to the design pattern give some indication of his level of visuospatial conceptualization. At the highest level is the patient who comprehends the design problem at a glance (forms a *gestalt* or unified concept) and scarcely looks at it again while putting the blocks together rapidly and correctly. Patients taking a little longer to study the design, who perhaps try out a block or two before proceeding without further hesitancy, or who refer back to the design continually as they work, function at a next lower level of conceptualization. Trial and error approaches contrast with the *gestalt* performance. In these the subject works from block to block, trying out and comparing his positioning of each block with the design before proceeding to the next one. This kind of performance is typical of persons in the *average* ability range. These people may never perceive the design as a total configuration, nor even appreciate the squared format, but by virtue of accurate perception and orderly work habits, many can solve even the most difficult of the design problems. Most people of *average* or better ability do form immediate *gestalts* of at least five of the easiest designs and then automatically shift to a trial and error approach at the point that the complexity of the design surpasses their conceptual level. Thus, another indicator of ability level on this perceptual organization task is the level of the most difficult design that the subject comprehends immediately.

The patient's problem-solving techniques reflect his work habits. Orderliness and planning are among the characteristics of working behavior that the block-manipulating format makes manifest. Some patients always work in the same direction, from left to right and up to down, for example, whereas others tackle whatever part of the design meets their eye and continue in *helter-skelter* fashion. Most subjects quickly appreciate that each block is identical, but some turn around each new block they pick up, looking for the desired side, and if it does not turn up at first they will set that block aside for another one. Some work so hastily that they misposition blocks and overlook errors through carelessness, whereas others may be slow but so method-

ical that they never waste a movement. Ability to perceive errors and willingness to correct them are also important aspects of the patient's work habits that can be readily seen on Block Design.

Temperamental characteristics, such as cautiousness, carefulness, impulsivity, impatience, apathy, etc., appear in the manner in which the patient responds to the problems. Self-deprecatory or self-congratulatory statements, requests for help, rejection of the task and the like betray the patient's feelings about himself.

The examiner should record significant remarks as well as the kinds of errors and manner of solution. For quick, successful solutions, he usually needs to note only whether the approach was conceptual or trial and error, and if trial and error, whether it was methodical or random. To some extent, time taken to solve a design will also indicate the patient's conceptual level and working efficiency since gestalt solutions generally take less time than those solved by methodical trial and error, which, in turn, generally are quicker than random trial and error solutions. It thus makes sense that high scores on this test depend to some extent on speed, particularly for younger subjects. For example, persons under the age of 35 cannot get scores above the 75th percentile (i.e., above the *average* range) without earning time credits. The examiner can document the patient's difficulties, his false starts, and incorrect solutions by sketching them on the margin of the Record Form, on a piece of paper kept handy for this purpose, or on a supplemental form that provides spaces for recording the designs. Of particular value in understanding and describing the patient's performance are sequential sketches of the evolution of a correct solution out of initial errors or of the compounding of errors and snowballing confusion of an ultimately failed design (e.g., Fig. 3-4a, p. 57).

Block Design is generally recognized as the best measure of visuospatial organization in the Wechsler scales. It reflects general ability to a moderate extent so that intellectually capable but academically or culturally limited persons frequently obtain their highest score on this test.

Block Design scores tend to be lower in the presence of any kind of brain injury. They are likely to be least affected when the lesion is confined to the left hemisphere, except when the left parietal lobe is involved (McFie, 1975). They tend to be moderately depressed by diffuse or bilateral brain lesions such as those resulting from traumatic injuries or diffuse degenerative processes that do not primarily involve cortical tissue.

Patients with diffuse loss of cortical neurons like that which characterizes Alzheimer's disease, severe damage to prefrontal cortex, or extensive right hemisphere damage that includes the parietal lobe are all likely to perform very poorly on this test, but in different ways (e.g., Luria, 1973). In the very early stages of the disease, Alzheimer's patients will understand the task and may be able to copy one or two designs. However, these patients soon get so confused between one block and another or between their constructions and the examiner's model that they may even be unable to imitate the placement of just one or two blocks. The quality of "stickiness," often used to describe the performance of organically impaired patients but hard to define, here takes on concrete meaning when patients place their blocks on the design

cards or adjacent to the examiner's model and appear unable to respond in any other way.

Patients with severe damage to the frontal lobes may display a similar stickiness despite assertions that they understand the task. With less severe damage, frontal lobe patients may fail items because of impulsivity and carelessness, a concrete perspective that prevents logical analysis of the designs with resulting random approaches to solving the problem or not seeing or correcting errors. Concrete thinking tends to show up in the first item, for such patients will try to make the sides as well as the top of their construction match that of the model; some even go so far as to lift the model to make sure they have matched the underside as well. These patients may be able to copy many of the designs quickly and accurately, but tend to fail item 8 (7 of the WAIS-R), for instance, by laying out red and white stripes with whole blocks rather than abstracting the 3×3 format and shifting their conceptualization of the design (from the mostly squared format of the first 3×3 design) to a solution based on diagonals.

The Alzheimer's patients and those frontal lobe patients who cannot make the blocks do what they want them to do can be properly described as having *constructional apraxia*. The discontinuity between intent, typically based on accurate perceptions, and action reflects the breakdown in the program of an activity that is central to the concept of apraxia.

Slowness in learning new response sets may develop with a number of conditions such as aging, a dementing process, frontal lobe disease, or head injury. The Block Design format is sufficiently unfamiliar that patients capable of performing well may do poorly at first if they have this problem. Since the first five items (four on the WAIS-R) are quite easy for persons with *average* or better constructional ability, they give the patient who is slow to learn a new set the opportunity to gain needed familiarity. These patients tend to display an interesting response pattern in which the first two items are failed or, at best, passed only on the second trial while the succeeding two or three or more items are passed, each more rapidly than the last. Those patients who are slow in learning a response set but whose ability to make constructions is good may succeed on most or even all the difficult items despite their early failure.

Block Design deficits associated with lateralized lesions are usually most common and most pronounced when the lesions involve posterior, particularly parietal, areas and are on the right side (Black and Strub, 1976; Newcombe, 1969; A. Smith, 1966b). Defective block design constructions made by patients with lesions in either hemisphere or when—under experimental conditions—a "split-brain" patient can use only one hemisphere, demonstrate that each hemisphere contributes to the realization of the design: "neither hemisphere alone is competent in this task" (Geschwind, 1979). However, the nature of the impairment tends to differ according to the side of the lesion (Consoli, 1979) (See pp. 285–286 for a discussion of these differences as they show up in relationships of scores on Block Design and Object Assembly to one another and to performances on purely visuo-perceptual tests.)

Patients with left, particularly parietal, lesions tend to show confusion, simplification, and concrete handling of the design. However, their approach is likely to be

orderly, they typically work from left to right as do intact subjects, and their construction usually preserves the square shape of the design. Their greatest difficulty is likely to be in placing the last block (which will typically be on their right) (McFie, 1975).

Patients with right-sided lesions may begin at the right of the design and work left. Their visuospatial deficits show up in disorientation, design distortions, and misperceptions. Some patients with severe visuospatial deficits lose sight of the squared or self-contained format of the design altogether (see Fig. 3-1a, p. 57). Left visuospatial inattention may compound these design-copying problems, resulting in two- or three-block solutions to the four-block designs, in which the whole left half or one left quadrant of the design has been omitted.

Both right and left hemisphere damaged patients make many more errors on the side of the design contralateral to the side of the lesion. Edith Kaplan has called attention to the importance of noting whether errors tend to occur more at the top or at the bottom of the constructions, as the upper visual fields have temporal lobe components while the lower fields have parietal components. Thus, a pattern of errors clustering at the top or at the bottom can also give some indication of the site and extent of the lesion.

PICTURE ARRANGEMENT

This test consists of eight sets (WAIS) or ten sets (WAIS-R) of cartoon pictures that make up stories. Each set is presented to the subject in scrambled order with instructions to rearrange the pictures to make the most sensible story (see Fig. 9-4). There are from three to six pictures in each set. Presentation is in order of increasing difficulty. Unless the subject fails both the first and second sets, all eight WAIS sets are administered. On the WAIS-R testing is discontinued after four consecutive failures. All but seriously retarded adults can do the first set (Matarazzo, 1972). Time limits range from one minute on the easiest items to two minutes on the two most difficult items. On five of the sets in each test there are two levels of accuracy. The subject can also earn time bonuses on the last two sets of the WAIS. Below age 55, the subject



Fig. 9-4. WAIS-type Picture Arrangement subtest item.

PARTICIPANT NUMBER _____ TEST DATE _____ AGE _____

WAIS-R RECORD FORM

Wechsler Adult Intelligence Scale Revised

PARTICIPANT NAME _____

REMARKS _____

DO NOT
MARK
IN
THIS
AREA

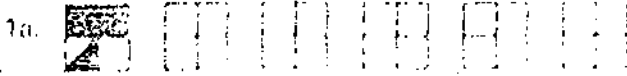
INFORMATION	SCORE
1. Floor	0 or 1
2. Ball	1
3. Moon	1
4. Thursday	1
5. Six	1
6. President	1
7. Venice	1
8. Amsterdam	1
9. Panama	1
10. Letter Day	1
11. Brazil	1
12. Yacht	1
13. October	1
14. Soviet	1
15. Canada	1
16. Italy	1
17. King	1
18. Congress	1
19. Sahara	1
20. Relativity	1
21. Yeast	1
22. Senators	1
23. Paris	1
24. Blood vessels	1
25. Temperature	1
26. Cone	1
27. Population	1
28. Koran	1
29. Easter	1

TEST	AGE	TEST	TESTER	SCORER
NO.	SCALE	NO.	CODE	CODE
0	0	0	0	0
1	1	1	1	1
2	2	2	2	2
3	3	3	3	3
4	4	4	4	4
5	5	5	5	5
6	6	6	6	6
7	7	7	7	7
8	8	8	8	8
9	9	9	9	9

WAIS-R: For use with the Wechsler Adult Intelligence Scale - Revised
 Copyright 1981, 1955, 1947 by The Psychological Corporation. All rights reserved. Adapted and reproduced by permission.

COMPLETED? YES NO TERMINATED REFUSED

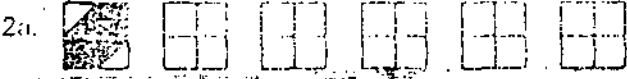
Block design apparatus consists of a set of 15 designs, each of a different or sequential approximation. Number placement of block design configurations is shown. To be made from 12 1/2" x 12 1/2" card inside down, no. 5 is at top of paper. Each grid represents a 30° angle and is 15.00 cm wide by 15.00 cm high.



Time: _____



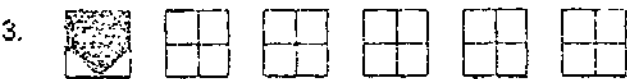
Time: _____



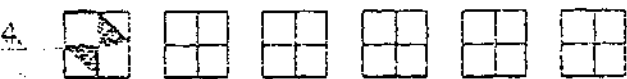
Time: _____



Time: _____



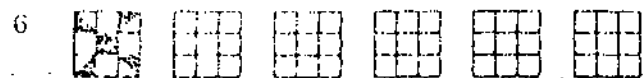
Time: _____



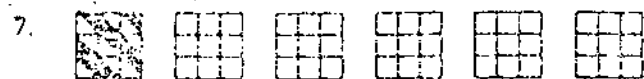
Time: _____



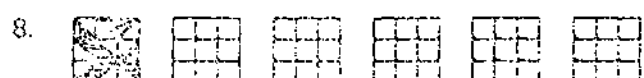
Time: _____



Time: _____



Time: _____



Time: _____



Time: _____

BLOCK DESIGN Discontinue after 3 consecutive failures

TOTAL - MAX 51 AGE SCALE SCORE

Design	TIME	Pass-Fail	SCORE
	Write time here & mark bubbles		Mark the appropriate score for each design.
1	10 20 30 40 50 60 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨		2
60"	10 20 30 40 50 60 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨	0 1	
2	10 20 30 40 50 60 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨		2
60"	10 20 30 40 50 60 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨	0 1	
3	10 20 30 40 50 60 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨		0 4 5 6
60"	10 20 30 40 50 60 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨	0	4 5 6
5	10 20 30 40 50 60 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨		4 5 6 7
60"	10 20 30 40 50 60 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨	0	4 5 6 7
6	10 20 30 40 50 60 70 80 90 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨		36 120 24 25 21 26 1 25
120"	10 20 30 40 50 60 70 80 90 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨	0	4 5 6 7
7	10 20 30 40 50 60 70 80 90 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨		4 5 6 7
120"	10 20 30 40 50 60 70 80 90 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨	0	4 5 6 7
8	10 20 30 40 50 60 70 80 90 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨		70 120 56 75 41 56 1 40
20"	10 20 30 40 50 60 70 80 90 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨	0	4 5 6 7
9	10 20 30 40 50 60 70 80 90 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨		70 120 56 75 41 56 1 40
120"	10 20 30 40 50 60 70 80 90 ① ② ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨	0	4 5 6 7

TEST NO	TESTER CODE	SCORER CODE
0	0	0
1	1	1
2	2	2
3	3	3
4	4	4
5	5	5
6	6	6
7	7	7
8	8	8
9	9	9

DO NOT MARK IN THIS SHADED AREA

7. WORD LIST GENERATION

1) Word List Generation: This measure assesses language system functioning, speed of word retrieval from memory, and general vocabulary. A subject has to generate as many words as possible that begins with a specific set of letters (F,A,S) for 60 second. This score is the number of words across the 3 letters.

(label)

+

+

EXAM CODE

(0001-0004)

/R/F/0/1/

Participant ID

(0005-0011)

//////

Participant Name

Date

(0012-0013)

///

Day

(0014-0015)

///

Year

(0016-0017)

///

Time Started

Hour

(0018-0019)

///

Min

(0020-0021)

///

Interviewer ID

(0022-0023)

///

Supervisor ID

(0024-0025)

///

A 'F' words

1-14 sec

1. no. of unique words /_/_/ (0030-0031)

2. no. of incorrect words /_/_/ (0032-0033)

98 = don't know
99 = refused

15-29 sec

3. no. of unique words /_/_/ (0034-0035)

4. no. of incorrect words /_/_/ (0036-0037)

98 = don't know
99 = refused

30-44 sec

5. no. of unique words /_/_/ (0038-0039)

6. no. of incorrect words /_/_/ (0040-0041)

98 = don't know
99 = refused

45-60 sec

7. no. of unique words /_/_/ (0042-0043)

8. no. of incorrect words /_/_/ (0044-0045)

98 = don't know
99 = refused

18) WORDS

1-14 sec

9. no. of unique words

///

(0046-0047)

10. no. of incorrect words

///

(0048-0049)

98 = don't know
99 = refused

15-29 sec

11. no. of unique words

///

(0050-0051)

12. no. of incorrect words

///

(0052-0053)

98 = don't know
99 = refused

30-44 sec

13. no. of unique words

///

(0054-0055)

14. no. of incorrect words

///

(0056-0057)

98 = don't know
99 = refused

45-60 sec

15. no. of unique words

///

(0058-0059)

16. no. of incorrect words

///

(0060-0061)

98 = don't know
99 = refused

18' words

1-14 sec

17. no. of unique words /_/_/ (0062-0063)

18. no. of incorrect words /_/_/ (0064-0065)

98 = don't know

99 = refused

15-29 sec

19. no. of unique words /_/_/ (0066-0067)

20. no. of incorrect words /_/_/ (0068-0069)

98 = don't know

99 = refused

30-44 sec

21. no. of unique words /_/_/ (0070-0071)

22. no. of incorrect words /_/_/ (0072-0073)

98 = don't know

99 = refused

45-60 sec

23. no. of unique words /_/_/ (0074-0075)

24. no. of incorrect words /_/_/ (0076-0077)

98 = don't know

99 = refused

C. Animal Words

1-14 sec

25. no. of unique words _/_/_/ (0078-0079)

26. no. of incorrect words _/_/_/ (0080-0081)

98 = don't know
99 = refused

15-29 sec

27. no. of unique words _/_/_/ (0082-0083)

28. no. of incorrect words _/_/_/ (0084-0085)

98 = don't know
99 = refused

30-44 sec

29. no. of unique words _/_/_/ (0086-0087)

30. no. of incorrect words _/_/_/ (0088-0089)

98 = don't know
99 = refused

45-60 sec

31. no. of unique words _/_/_/ (0090-0091)

32. no. of incorrect words _/_/_/ (0092-0093)

98 = don't know
99 = refused

33. Comment

_____ (0094-0124)

DESCRIBE ANY UNUSUAL FINDINGS THAT COULD INFLUENCE THIS TEST

8. CALIFORNIA VERBAL LEARNING TEST

5) California Verbal Learning Test (CVLT) Total Learning Score:

This test assesses active verbal learning and memory ability by requiring the subject to recall 16 words over 5 learning trials. This score represents the total number of words recalled over these 5 trials.

6) California Verbal Learning Test (CVLT) Short-Term Recall

Score: This component of the CVLT assesses a subject's ability to recall the 16 words previously learned after they had been given another group of words to learn. This score is the number of total words (out of 16) recalled.

7) California Verbal Learning Test (CVLT) Percent Change score

from short-term recall to long-term recall: This score is a measure of long-term memory abilities. It is the percentage of the 16 original words recalled after a 20 minute period compared to the number recalled on short-term recall. Negative numbers represent the percentage decline in recall over this time period.

THE CALIFORNIA VERBAL LEARNING TEST: ADMINISTRATION
AND INTERPRETATION¹

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and

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Notice: Preliminary Manual

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THE CALIFORNIA VERBAL LEARNING TEST: ADMINISTRATION
AND INTERPRETATION

INTRODUCTION

In clinical neuropsychology, the most commonly used tests of memory are widely criticized as having serious deficiencies (Lezak, 1983; Russell, 1981; Parson & Prigatano, 1977). The shortcomings ascribed to these tests include their failure to assess retention of information for periods longer than a few seconds, their confounding of the assessment of memory skills with other cognitive abilities, and their failure to provide quantitative measures of the multiple underlying processes of memory functioning. A primary reason for these shortcomings is that existing memory tests employ an achievement scoring system which quantifies performance in terms of some pass/fail criterion. Such an approach culminates in a single score, and fails to measure different types of learning processes, errors, and strategies (see Kaplan, 1983, for a discussion of achievement versus process analyses in neuropsychological assessment).

The lack of sophisticated memory tests in clinical neuropsychology is a serious problem, since almost all types of brain pathology will in some way affect the ability to learn and remember information (Luria, 1981; Goodglass & Kaplan, 1979), and since a brain-injured patient's ability to live independently and to return to his² former occupation will largely depend, among other factors, on his verbal memory skills (Lezak, 1983). In addition, the rapidly developing field of cognitive rehabilitation is in need of more sensitive procedures to (1) delineate the specific memory problems of individual patients; (2) direct the rehabilitation effort; and (3) monitor the efficacy of the intervention. Memory is one of the most complex processes of brain functioning (Luria, 1981), and extant memory tests have not

ressed this complexity.

Designed to incorporate findings from both the clinical and experimental memory literature, the California Verbal Learning Test (CVLT; see Appendix A) utilizes a process scoring system to provide quantitative measures of multiple parameters of memory. The CVLT assesses not only the amount of verbal material a patient learns, but also such process data as the rate of learning over several trials, the encoding strategy used, the types of errors made, the vulnerability of memory to varying delays in time and to interference conditions, and the degree to which memory performance improves with assisted recall (e.g., when the patient is given categorical cues).

The basic format of the CVLT was modeled after the Rey Auditory Verbal Learning Test (Rey, 1964; Lezak, 1983). Rey's test evaluates an individual's ability to learn a list of 15 unrelated words over five trials. A new list of 15 unrelated words is then presented once, immediately followed by a recall of words and a recognition test for the first list. The assessment of retention of the first list after the presentation of the second list enables an evaluation of forgetting in the face of interference, both when retrieval is required (free recall) and when discrimination between target items and new distractor items is required (recognition).

The CVLT adds to this format several other testing and scoring features:

ECOLOGICAL VALIDITY: The CVLT is designed to be similar to a task a person is likely to encounter in his everyday life. Thus, rather than presenting a list of randomly selected words, the CVLT uses items which could make up a shopping list. The testing is therefore made more relevant for the patient, and inferences about how a patient approaches a memory

SHORT DELAY FREE RECALL
Now I'd like you to tell me all of the shopping items you can from the Monday list.

SHORT DELAY CUED RECALL
Tell me all of the shopping items from the Monday list that are: (Category)

LONG DELAY FREE RECALL
I read some shopping items to you earlier. I'd like you to tell me all the items you can from the Monday list - that was the first list I gave you.

LONG DELAY CUED RECALL
Tell me all of the shopping items from the Monday List that are: (Category)

SPICES & HERBS

TOOLS

SPICES & HERBS

TOOLS

FRUITS

CLOTHING

FRUITS

CLOTHING

Time of Day Long Term Free Recall Begun:

Time of Day Short Term Cued Recall Completed:

Total Delay

LONG DELAY RECOGNITION

I'm going to read a list of shopping items. After I read each item, say 'yes' if the item was from the Monday list and 'no' if it was not.

	M	TR	TU	NR	NU	PS
Sweater	*	*	*	*	*	*
Oregano	*	*	*	*	*	*
Flounder	*	*	*	*	*	*
Rug	*	*	*	*	*	*
Tires	*	*	*	*	*	*
Pepper	*	*	*	*	*	*
Jacket	*	*	*	*	*	*
Aspirin	*	*	*	*	*	*
Wax	*	*	*	*	*	*
Drill	*	*	*	*	*	*
Apricots	*	*	*	*	*	*
Spatula	*	*	*	*	*	*
Cherries	*	*	*	*	*	*
Drum	*	*	*	*	*	*
Chives	*	*	*	*	*	*
Film	*	*	*	*	*	*
Chisel	*	*	*	*	*	*
Brulcase	*	*	*	*	*	*
Pastry	*	*	*	*	*	*
Tangerines	*	*	*	*	*	*
Clock	*	*	*	*	*	*
Shoes	*	*	*	*	*	*
Grapes	*	*	*	*	*	*
Salmon	*	*	*	*	*	*
Paprika	*	*	*	*	*	*
Racket	*	*	*	*	*	*
Ginger	*	*	*	*	*	*
Stacks	*	*	*	*	*	*
Books	*	*	*	*	*	*
Parsley	*	*	*	*	*	*
Vest	*	*	*	*	*	*
Apples	*	*	*	*	*	*
Grill	*	*	*	*	*	*
Plums	*	*	*	*	*	*
Wrench	*	*	*	*	*	*
Lemons	*	*	*	*	*	*
Tapes	*	*	*	*	*	*
Vestamins	*	*	*	*	*	*
Pliers	*	*	*	*	*	*
Bowl	*	*	*	*	*	*
Hammer	*	*	*	*	*	*
Nutmeg	*	*	*	*	*	*
Chimes	*	*	*	*	*	*
Soap	*	*	*	*	*	*

/ CORR
 / TR /4
 / TU /4
 / NR /4
 / NU /8
 / PS /8

Participant No. _____ Participant Name _____
 Technician No. _____ Completion _____ 1-Yes; 2-No; 7-Terminated; 9-Refused

Test Date _____ Test No. _____ Debriefed _____ Score No. _____

9. REY OSTERREITH COMPLEX FIGURE DRAWING

8) Rey Osterreith Complex Figure Drawing - Copy Score: This test is a drawing test which requires the subject to reproduce a complex figure. It assesses visual-perceptual-motor, visual-spatial, planning and organizational skills. Scoring is based on the number of components in the design that are correctly drawn.

9) Rey Osterreith Complex Figure Drawing - Short-Term Recall: This score is based on the subject's ability to redraw the design from memory after they copy it. As they are not told they will have to do this, this score is considered to test incidental learning and short-term memory of visual-spatial information.

10) Rey Osterreith Complex Figure Drawing - Percentage Change Score on long-term recall: This score is a measure of a subject's memory for the complex figure after a 20 minute delay. It compares their score on long-term recall with their score on short-term recall. A negative score represents the percentage decline in recall over time.

were controlled, this test proved worthless (Helmes et al., 1980). Cultural background may also influence performance on this test (D. M. Harrison and Chagnon, 1966).

THE COMPLEX FIGURE TEST (CFT): COPY ADMINISTRATION

A "complex figure" was devised by Rey (1941) to investigate both perceptual organization and visual memory in brain damaged subjects. (See pp. 444-447 for a discussion of the complex figure in memory testing.) Osterrieth (1944) standardized Rey's procedure, obtaining normative data from the performance of 230 normal children of ages ranging from four to 15 and 60 adults in the 16-60 age range. In addition to two groups of children with learning and adjustment problems, he studied a small number of behaviorally disturbed adults, 43 who had sustained traumatic brain injury, and a few patients with endogenous brain disease. More recently, L. B. Taylor made up an alternate complex figure for use in retesting (Milner, 1975; L. B. Taylor, 1969, 1979). Although normative data have not been obtained for the Taylor figure, its comparability to the Rey figure in design elements and complexity is reflected in the similarity of scores obtained on retest by patients with left temporal lobectomies whose drawing abilities, ordinarily, are unaffected by left temporal epileptic foci or surgery for this condition.

The test material consists of Rey's complex figure (see Fig. 13-2) or Taylor's complex figure (see Fig. 13-3), blank typewriter-size paper, and five or six colored pens or pencils. The subject is first instructed to copy the figure, which has been so set out that its length runs along the subject's horizontal plane. The examiner watches the subject's performance closely. Each time the subject completes a section of the drawing, the examiner hands him a different colored pencil and notes the order of the colors. Instead of using color for tracking the subject's performance, some examiners keep a detailed record of the subject's copying sequence by reproducing the performance, numbering each unit in the order that it is drawn (Binder, 1982; Edith Kaplan, personal communication). Visser (1973) uses a "registration sheet" containing the printed Rey figure, which the examiner numbers in the order in which the subject makes his copy. This latter method is a satisfactory and effort-saving procedure except when the subject produces a drawing that deviates significantly from the original. When this happens, Visser's instructions to ignore extra lines and to deal with "wrongly placed [lines] . . . as if they were placed correctly" can result in a confusing and misleading record. For most clinical purposes, switching colors generally affords an adequate representation of the subject's overall approach. When using the CFT for research, the technique of drawing exactly what the subject draws and numbering each segment (I use directional arrows as well) will best preserve the drawing sequence accurately. Time to completion is recorded and both the test figure and the subject's drawings are removed. This is usually followed by one or more recall trials. Some subjects who are dissatisfied with a poorly executed copy show improvement on a second copy trial.

Osterrieth analyzed the drawings in terms of the patient's method of drawing as well as specific copying errors. He identified seven different procedural types: (I) Sub-

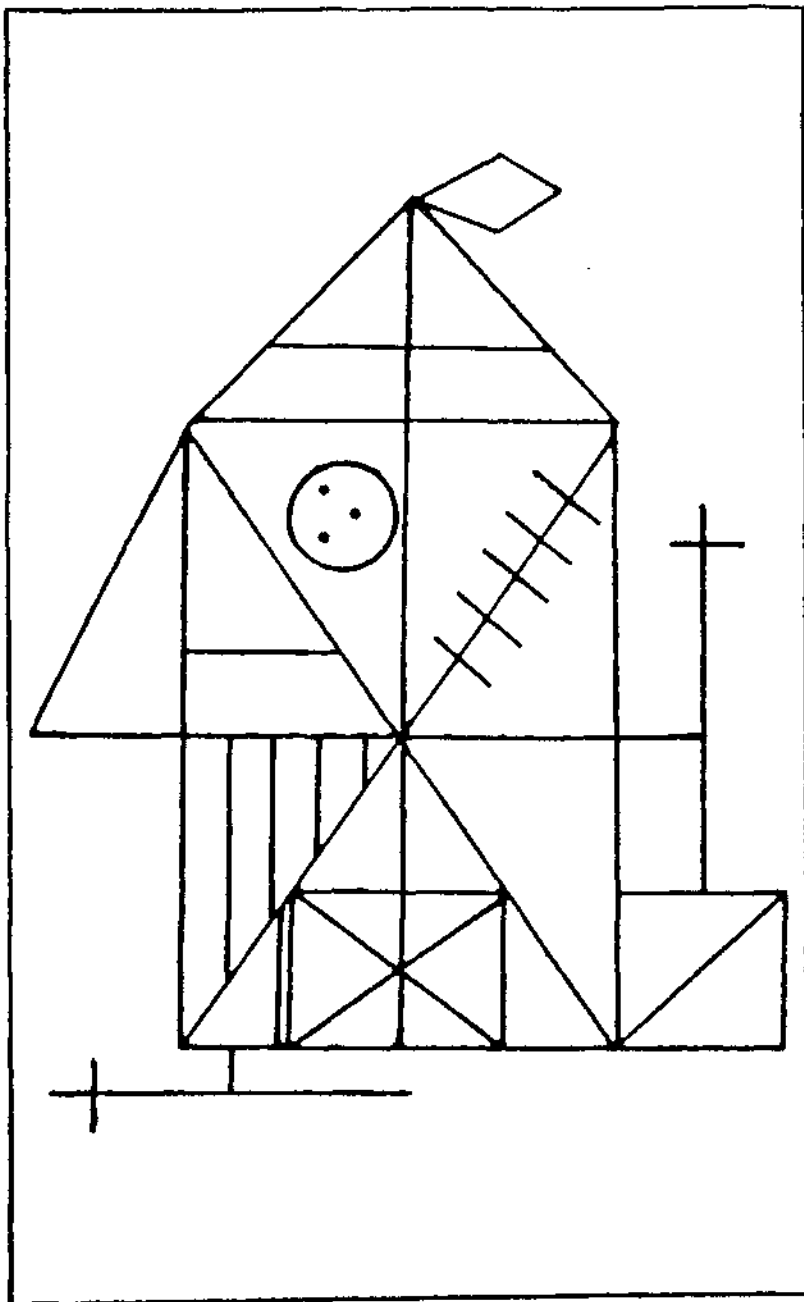


Fig. 13-2 Rey Complex Figure (Osterrieth, 1944).

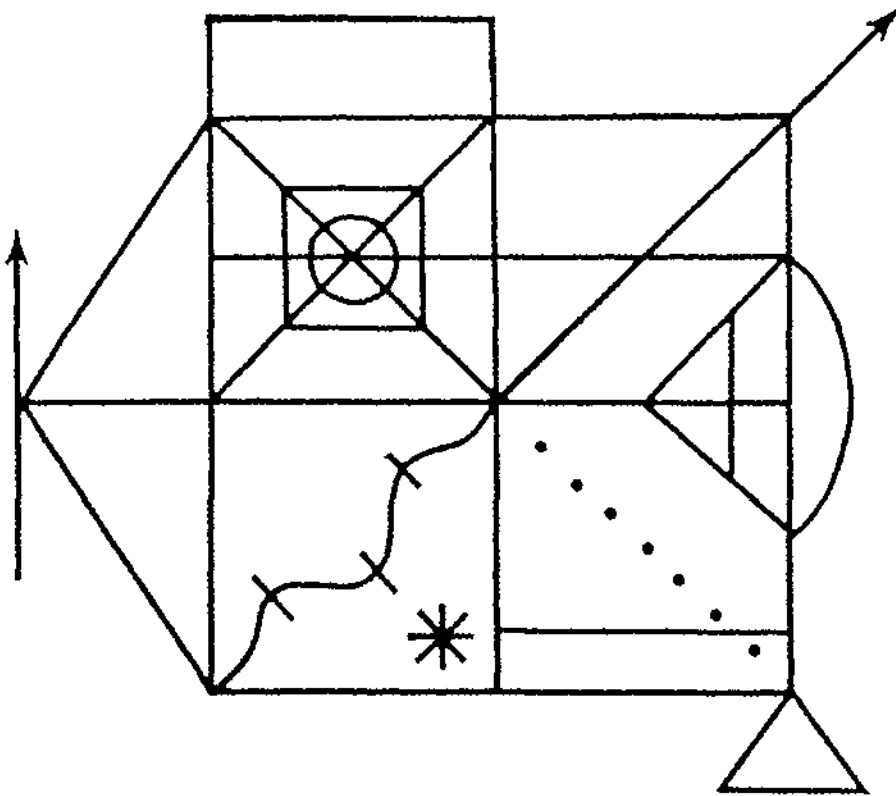


Fig. 13-3. Taylor Complex Figure (actual size).

ject begins by drawing the large central rectangle and details are added in relation to it. (II) Subject begins with a detail attached to the central rectangle, or with a subsection of the central rectangle, completes the rectangle and adds remaining details in relation to the rectangle. (III) Subject begins by drawing the overall contour of the figure without explicit differentiation of the central rectangle and then adds the internal details. (IV) Subject juxtaposes details one by one without an organizing structure. (V) Subject copies discrete parts of the drawing without any semblance of organization. (VI) Subject substitutes the drawing of a similar object, such as a boat or house. (VII) The drawing is an unrecognizable scrawl.

In Osterrieth's sample, 83% of the adult control subjects followed procedure Types I and II, 15% used Type IV, and there was one Type III Subject. Past the age of seven, no child proceeded on a Type V, VI, or VII basis, and from age 13 onward, more than half the children followed Types I and II. No one, child or adult, produced a scrawl. More than half (63%) of the traumatically brain injured group also followed Type I and II procedures, although there were a few more Type III and IV subjects in this group and one of Type V. Three of four aphasic patients and one with senile

dementia gave Type IV performances; one aphasic and one presenile dementia patient followed a Type V procedure.

In line with Osterreith's observations, Visser (1973) noted that "brain-damaged subjects deviate from the normals mainly in the fact that the large rectangle does not exist for them . . . [Thus] since the main line clusters do not exist, (parts of) the main lines and details are drawn intermingled, working from top to bottom and from left to right" (p. 23).

Although, like all overgeneralizations, Visser's statement has exceptions, Binder (1982) showed how stroke patients tend to lose the overall configuration of the design. By analyzing how subjects draw the structural elements of the Rey-Osterreith figure (the vertices of the pentagon drawn together, horizontal midline, vertical midline, and two diagonals) (Fig. 13-4). Binder obtained three scores: Configural Units is the number of these five elements that were each drawn as one unit; Fragmented Units is the number that were not drawn as a unit (this is not the inverse of the Configural score as it does not include incomplete units, i.e., those that had a part missing); and Missing Units is the number of incomplete or omitted units. Fourteen patients with left brain damage tended to display more fragmentation (mean score of 1.64) than the 14 with right-sided lesions (mean score of 0.71), but the latter group's average Missing Units score of 1.71 (primarily due to left-sided neglect) far outweighed a negligible Missing Units score of 0.07 for the left CVA group. In contrast, 14 normal control subjects averaged 0.21 Fragmented Units and omitted none. These copying approaches were reflected in the low Configural Unit average of 2.57 for patients with right-sided CVAs, a higher average Configural Unit score of 3.29 for those with left CVAs, and a near-perfect average score of 4.79 achieved by the control subjects.

Visser (1973) suggests that the fragmented or piecemeal approach to copying the complex figure that is so characteristic of brain damaged persons reflects their inabil-

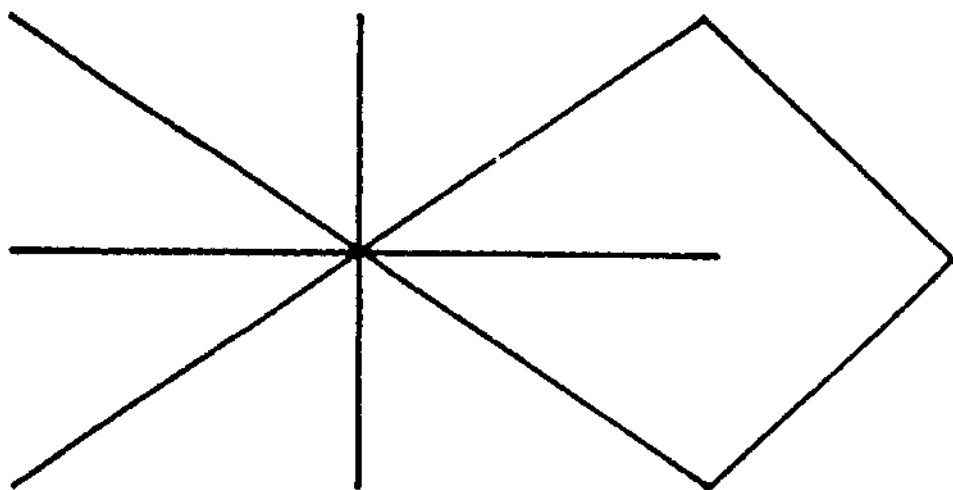


Fig. 13-4. Structural elements of the Rey Complex Figure (Binder, 1982).

ity to process as much information at a time as do normals. Thus, brain damaged persons tend to deal with smaller visual units, building the figure by accretion. Many ultimately produce a reasonably accurate reproduction in this manner, although the piecemeal approach increases the likelihood of size and relationship errors (Messerli et al., 1979).

Messerli and his colleagues (1979) looked at copies of the Rey figure drawn by 32 patients whose lesions were entirely or predominantly localized within the frontal lobes. They found that, judged overall, 75% differed significantly from the model. The most frequent error (in 75% of the defective copies) was the repetition of an element that had already been copied, an error resulting from the patient's losing track of what he had drawn where because of a disorganized approach. In one-third of the defective copies, a design element was transformed into a familiar representation (e.g., the circle with three dots was rendered as a face). Perseveration occurred less often, usually showing up as additional cross-hatches (scoring unit 12) or parallel lines (scoring unit 8). Omissions were also noted.

Laterality differences in approach to these drawings emerge in several ways. Binder's study (1982) showed that patients with left hemisphere damage tend to break up the design into units that are smaller than normally perceived while right hemisphere damage makes it more likely that elements will be omitted altogether. However, on recall of the complex figure, patients with left hemisphere damage who may have copied the figure in a piecemeal manner tend to reproduce the basic rectangular outline and the structural elements as a configural whole, suggesting that their processing of all these data is slow but, given time, they ultimately reconstitute the data as a gestalt. This reconstitution is less likely to occur with right hemisphere damaged patients who, on recall, continue to construct poorly integrated figures (also see Chapter 14, pp. 445-446). Archibald (no date) found that, overall, patients with left-sided lesions tend to make more simplifications in their copies than do patients with right-sided lesions. These two groups differ in that the simplifications of patients with right brain damage involve partial omissions (e.g., fewer dots or lines than called for) while left brain damaged patients tend to simplify by rounding angles (e.g., giving curved sides to the diamond of the Rey figure), drawing dashes instead of dots, which are more difficult to execute, or leaving the cross of the Rey figure in an incomplete, T-shaped form. Of the 32 simplifications made by patients with left hemisphere damage, however, only five were made with the right hand, and three of these errors were made by patients who had residual right upper limb weakness. All others were made by the nonpreferred (left) hand of hemiparetic patients. These data suggest that, for the most part, simplification errors of patients with left hemisphere damage are the product of the left hand's deficient control over fine movements; i.e., simplification in patients with left-sided lesions is a defect of execution, not one of perception or cognition. Binder's right and left hemisphere damaged patients also differed significantly in the accuracy of their reproductions. Patients with right hemisphere damage produced much less accurate copies than patients with left CVAs who, although on the whole less accurate than the normal control group, still showed some overlap in accuracy scores with the control group.

Differences between patients with parietal-occipital lesions and patients with fron-

tal lobe damage were demonstrated in their failures to copy the complex figure correctly (Pillon, 1981b). Errors made by the frontal patients reflected disturbances in their ability to program the approach to copying the figure. Patients with parietal-occipital lesions, on the other hand, had difficulty with the spatial organization of the figure. When given a plan to guide their approach to the copy task, the patients with frontal damage improved markedly. The patients with posterior lesions also improved their copies when provided spatially reference points. However, use of spatial reference points did not improve the copies made by the patients with frontal damage, nor did those with parietal-occipital lesions benefit from a program plan.

Overall evaluations of the success of a drawing of the complex figure can be obtained by using an accuracy score based on a unit scoring system (see Tables 13-3 and 13-4). The scoring units refer to specific areas or details of the figures that have been numbered for scoring convenience. Since the reproduction of each unit can earn as many as two score points, the highest possible number of points is 36. From age

Table 13-3 Scoring System for the Rey Complex Figure

Units

1. Cross upper left corner, outside of rectangle
2. Large rectangle
3. Diagonal cross
4. Horizontal midline of 2
5. Vertical midline
6. Small rectangle, within 2 to the left
7. Small segment above 6
8. Four parallel lines within 2, upper left
9. Triangle above 2 upper right
10. Small vertical line within 2, below 9
11. Circle with three dots within 2
12. Five parallel lines within 2 crossing 3, lower right
13. Sides of triangle attached to 2 on right
14. Diamond attached to 13
15. Vertical line within triangle 13 parallel to right vertical of 2
16. Horizontal line within 13, continuing 4 to right
17. Cross attached to 5 below 2
18. Square attached to 2, lower left

Scoring

Consider each of the 18 units separately. Appraise accuracy of each unit and relative position within the whole of the design. For each unit count as follows:

Correct	} placed properly	2 points
		} placed poorly
Distorted or incomplete but recognizable	} placed properly	1 point
		} placed poorly
Absent or not recognizable		0 points
Maximum		36 points

(From E. M. Taylor, 1959, adapted from Osterrieth, 1944)

CONSTRUCTIONAL FUNCTIONS

Table 13-4 Scoring System for the Taylor Complex Figure

Units

1. Arrow at left of figure.
2. Triangle to left of large square.
3. Square, which is the base of figure.
4. Horizontal midline of large square, which extends to 1.
5. Vertical midline of large square.
6. Horizontal line in top half of large square.
7. Diagonals in top left quadrant of large square.
8. Small square in top left quadrant.
9. Circle in top left quadrant.
10. Rectangle above top left quadrant.
11. Arrow through and extending out of top right quadrant.
12. Semicircle to right of large square.
13. Triangle with enclosed line in right half of large square.
14. Row of 7 dots in lower right quadrant.
15. Horizontal line between 6th and 7th dots.
16. Triangle at bottom right corner of lower right quadrant.
17. Curved line with 3 cross-bars in lower left quadrant.
18. Star in lower left quadrant.

Scoring

Follow instructions given in Table 13-3 for scoring the Rey figure.

eight onward, the average score is 30 or above; the average adult's score is 32 (see Table 13-5). The accuracy score provides a good measure of how well the subject reproduces the design, regardless of the approach he uses. Since the memory trial of the CFT is scored in the same manner, the accuracy score permits a comparison between the different trials of the test (see Chapter 14, pp. 445, 447). For example, although almost half of the 43 traumatically brain injured adult patients in Osterrieth's sample achieved "copy" scores of 32 or better, one-third of this group's scores were significantly low. On the memory trial, fewer than one-third of the traumatically brain injured group were able to achieve the normal group's mean score of 22. In general, there was a wider disparity between the copy and memory scores of the brain injured group than in Osterrieth's normal group of 60 persons ages 16 to 60. Four patients performed relatively better on the memory than the copy task, suggesting delayed perceptual organization or slowed ability to adapt to new tasks. Seven patients diagnosed as having severe psychiatric disorders were the only adults to add

Table 13-5 Percentile Norms for Accuracy Scores Obtained by Adults on the Copy Trial of the Complex Figure Test

Percentile	10	20	30	40	50	60	70	80	90	100
Score	29	30	31	32	32	33	34	34	35	36

(Adapted from Osterrieth, 1944)

bizarre embellishments to their drawings, interpret details concretely, or fill in parts of the design with solid color. No behavior of this kind appeared among the brain damaged patients.

THE BENTON VISUAL RETENTION TEST (BVRT): COPY ADMINISTRATION (Benton, 1974)

The three alternate forms of this test permit the use of one of them for a copy trial. (See pp. 447-448 for a description and picture of the test.) The copy trial usually precedes the memory trials, which allows the subject to familiarize himself with the test and the test materials before undertaking the more difficult memory tests. Benton's normative population of 200 adults provides the criteria for evaluating the scores. Each patient's drawings must be evaluated in terms of his estimated original level of functioning. Persons of *average* or better intelligence are expected to make no more than two errors. Subjects making three or four errors who typically perform at *low average to borderline* levels on most other intellectual tasks have probably done as well as could be expected on this test; for them, the presence of a more than ordinary number of errors does not signify a visuographic disability. On the other hand, the visuographic functioning of subjects who achieve a cluster of test scores on other kinds of tasks in the ranges above *average* and who make four or five errors on this task is suspect.

The performance of patients with frontal lobe lesions differs with the side of injury: those with bilateral damage average 4.6 errors; with right-sided damage, 3.5 errors; and with left-sided damage the average 1.0 error is comparable to that of the normative group (Benton, 1968). Other studies tend to support a right-left differential in defective copying of these designs, with right hemisphere patients two or three times more likely to have difficulties (Benton, 1969a). However, in one study that included aphasic patients in the comparisons between groups with lateralized lesions, no differences were found in the frequency with which constructional impairment was present in the drawings of right and left hemisphere damaged patients (Arena and Gainotti, 1978).

MISCELLANEOUS COPYING TASKS

Since any copying task can produce meaningful results, the examiner should feel free to improvise tasks as he sees fit. He can learn to reproduce a number of useful figures and then draw them at bedside examinations or in interviews when his test material is not available. Hécaen and co-workers (1951) and Warrington (1970) give some excellent examples of how easily drawn material for copying, such as a cube, a Greek cross, and a house can contribute to the evaluation of visuographic disabilities (see Fig. 13-5). Bilaterally symmetrical models for copying such as the cross and the star in Figure 13-5, or the top left and bottom designs from the Stanford-Binet Scale (Fig. 14-2, p. 444) are particularly suited to the study of unilateral inattention.

Another simple copying technique that is sensitive to visual inattention as well as

REY OSTERRIETH COMPLEX FIGURE

PARTICIPANT NUMBER							
0	0	0	0	0	0	0	0
1	1	1	1	1	1	1	1
2	2	2	2	2	2	2	2
3	3	3	3	3	3	3	3
4	4	4	4	4	4	4	4
5	5	5	5	5	5	5	5
6	6	6	6	6	6	6	6
7	7	7	7	7	7	7	7
8	8	8	8	8	8	8	8
9	9	9	9	9	9	9	9

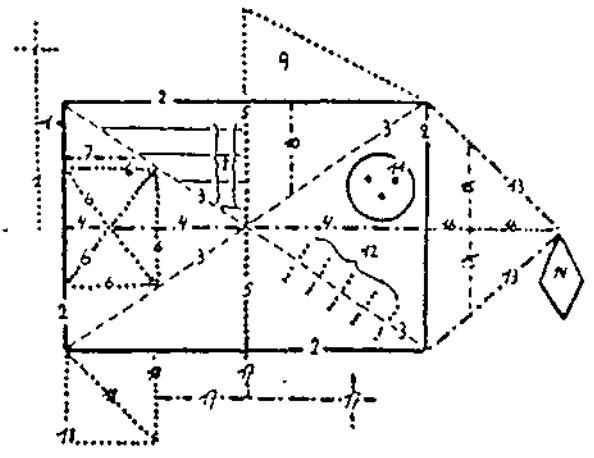
TEST DATE		
MONTH	DAY	YEAR
<input type="radio"/> JAN		
<input type="radio"/> FEB		
<input type="radio"/> MAR	0 0	0
<input type="radio"/> APR	1 1	1
<input type="radio"/> MAY	2 2	2
<input type="radio"/> JUN	3 3	3
<input type="radio"/> JUL	4	4
<input type="radio"/> AUG	5	5
<input type="radio"/> SEP	6	6
<input type="radio"/> OCT	7	7
<input type="radio"/> NOV	8 8	8
<input type="radio"/> DEC	9 9	9

TEST NO.
0 0
1 1
2 2
3
4
5
6
7
8
9

TESTER CODE				SCORER CODE			
0	0	0	0	0	0	0	0
1	1	1	1	1	1	1	1
2	2	2	2	2	2	2	2
3	3	3	3	3	3	3	3
4	4	4	4	4	4	4	4
5	5	5	5	5	5	5	5
6	6	6	6	6	6	6	6
7	7	7	7	7	7	7	7
8	8	8	8	8	8	8	8
9	9	9	9	9	9	9	9

PARTICIPANT NAME _____

REMARKS



	COPY	MEMORY	
		IMMEDIATE	DELAYED
1. Cross upper left corner, outside of rectangle	0 5 1 2	0 5 1 2	0 5 1 2
2. Large rectangle	0 5 1 2	0 5 1 2	0 5 1 2
3. Diagonal cross	0 5 1 2	0 5 1 2	0 5 1 2
4. Horizontal midline of 2	0 5 1 2	0 5 1 2	0 5 1 2
5. Vertical midline	0 5 1 2	0 5 1 2	0 5 1 2
6. Small rectangle, within 2 to the left	0 5 1 2	0 5 1 2	0 5 1 2
7. Small segment above 6	0 5 1 2	0 5 1 2	0 5 1 2
8. Four parallel lines within 2, upper left	0 5 1 2	0 5 1 2	0 5 1 2
9. Triangle above 2 upper right	0 5 1 2	0 5 1 2	0 5 1 2
10. Small vertical line within 2, below 9	0 5 1 2	0 5 1 2	0 5 1 2
11. Circle with three dots within 2	0 5 1 2	0 5 1 2	0 5 1 2
12. Five parallel lines with 2 crossing 3, lower right	0 5 1 2	0 5 1 2	0 5 1 2
13. Sides of triangle attached to 2 on right	0 5 1 2	0 5 1 2	0 5 1 2
14. Diamond attached to 13	0 5 1 2	0 5 1 2	0 5 1 2
15. Vertical line within triangle 13 parallel to right vertical of 2	0 5 1 2	0 5 1 2	0 5 1 2
16. Horizontal line within 13, continuing 4 to right	0 5 1 2	0 5 1 2	0 5 1 2
17. Cross attached to 5 below 2	0 5 1 2	0 5 1 2	0 5 1 2
18. Square attached to 2, lower left	0 5 1 2	0 5 1 2	0 5 1 2
	TOTAL ↴	TOTAL ↴	TOTAL ↴

SCORING

Consider each of the eighteen units separately. Appraise accuracy of each unit and relative position within the whole of the design. For each unit count as follows:

Correct	placed properly	2 points
	placed poorly	1 point
Distorted or incomplete but recognizable	placed properly	1 point
	placed poorly	½ point
Absent or not recognizable		0 point
Maximum		36 points

0	0	0
1	1	1
2	2	2
3	3	3
4	4	4
5	5	5
6	6	6
7	7	7
8	8	8
9	9	9

10. PACED AUDITORY SERIAL ADDITION TASK

13) Paced Serial Addition Test: This is a measure of mental control, mental speed, computational and attentional abilities. The subject is required to mentally add a sequence of numbers in rapid succession.

PACED AUDITORY SERIAL ADDITION TEST (PASAT) (Gronwall and Sampson, 1974;
Gronwall and Wrightson, 1974)

This sensitive test simply requires that the patient add 60 pairs of randomized digits so that each is added to the digit immediately preceding it. For example, if the examiner reads the numbers "2-8-6-1-9," the subject's correct responses, beginning as soon as the examiner says "8," are "10-14-7-10." The digits are presented at four rates of speed, each differing by 0.4 seconds and ranging from one every 1.2 seconds to one every 2.4 seconds. Precise control over the rate at which digits are read requires a taped presentation. Gronwall begins the tape with a brief repetition task that is followed by a ten-digit practice series presented at the 2.4-second rate. Sixty-one digits are given at each rate. The performance can be evaluated in terms of the percentage of correct responses or the mean score (see Table 17-4; the data are rounded to the nearest whole number).

Postconcussion patients consistently perform well below control group averages immediately after injury or return to consciousness. The overwhelming tendency is for their scores to return to normal within 30 to 60 days. Based on an evaluation of how the PASAT performance was associated with performances on memory and attention tasks, Gronwall and Wrightson (1981) concluded that the PASAT is very sensitive to deficits in information processing ability. By using the PASAT performance as an indicator of the efficiency of information processing following concussion, the examiner can determine when a patient is able to return to a normal level of social and vocational activity without experiencing undue stress, or when a modified activity schedule would be best (Gronwall, 1977).

Although this technique was developed for taped presentation in order to control the presentation rate, with practice the examiner should be able to deliver the numbers at a reasonably steady one or two second rate. The task can also be presented at

Table 17-4 Average PASAT Percent Correct and Mean Scores Made by Control Group at Four Presentation Rates

Presentation rate (seconds)	1.2	1.6	2.0	2.4
Average percent correct	51	66	73	82
Mean score (\pm SD)	22 \pm 5	32 \pm 8	40 \pm 7	46 \pm 6

(Adapted from Gronwall and Wrightson, 1974; Gronwall, 1977)

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A COMPENDIUM OF TESTS AND ASSESSMENT TECHNIQUES

the subject's response rate (i.e., unpaced), in which case the examiner should record pauses of five seconds and longer. Although the paced delivery format identifies patients whose responses are slowed as well as those who have a tracking disability, the unpaced delivery is more likely to identify those patients whose defective performance is due to a tracking defect.

PARTICIPANT NUMBER	TEST DATE			TEST NO	TECH CODE	SCORER CODE
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<input type="radio"/> 2	<input type="radio"/> MAR	<input type="radio"/> 0	<input type="radio"/> 0	<input type="radio"/> 2	<input type="radio"/> 2	<input type="radio"/> 2
<input type="radio"/> 3	<input type="radio"/> APR	<input type="radio"/> 1	<input type="radio"/> 1	<input type="radio"/> 3	<input type="radio"/> 3	<input type="radio"/> 3
<input type="radio"/> 4	<input type="radio"/> MAY	<input type="radio"/> 2	<input type="radio"/> 2	<input type="radio"/> 4	<input type="radio"/> 4	<input type="radio"/> 4
<input type="radio"/> 5	<input type="radio"/> JUN	<input type="radio"/> 3	<input type="radio"/> 3	<input type="radio"/> 5	<input type="radio"/> 5	<input type="radio"/> 5
<input type="radio"/> 6	<input type="radio"/> JUL	<input type="radio"/> 4	<input type="radio"/> 4	<input type="radio"/> 6	<input type="radio"/> 6	<input type="radio"/> 6
<input type="radio"/> 7	<input type="radio"/> AUG	<input type="radio"/> 5	<input type="radio"/> 5	<input type="radio"/> 7	<input type="radio"/> 7	<input type="radio"/> 7
<input type="radio"/> 8	<input type="radio"/> SEP	<input type="radio"/> 6	<input type="radio"/> 6	<input type="radio"/> 8	<input type="radio"/> 8	<input type="radio"/> 8
<input type="radio"/> 9	<input type="radio"/> OCT	<input type="radio"/> 7	<input type="radio"/> 7	<input type="radio"/> 9	<input type="radio"/> 9	<input type="radio"/> 9
<input type="radio"/> 0	<input type="radio"/> NOV	<input type="radio"/> 8	<input type="radio"/> 8	<input type="radio"/> 0	<input type="radio"/> 0	<input type="radio"/> 0
<input type="radio"/> 1	<input type="radio"/> DEC	<input type="radio"/> 9	<input type="radio"/> 9	<input type="radio"/> 1	<input type="radio"/> 1	<input type="radio"/> 1

PACED AUDITORY SERIAL ADDITION TASK

PARTICIPANT NAME _____

REMARKS _____

SERIES 1 ISI - 2.4 Sec	CORRECT RESPONSE	PARTICIPANT'S RESPONSE	0 = WRONG 1 = RIGHT	SCORES	SERIES 2 ISI - 2.5 Sec	CORRECT RESPONSE	PARTICIPANT'S RESPONSE	0 = WRONG 1 = RIGHT	SCORES
1	9		<input type="radio"/> 0 <input type="radio"/> 1		1	2		<input type="radio"/> 0 <input type="radio"/> 1	
2	1	10	<input type="radio"/> 0 <input type="radio"/> 1		2	4	6	<input type="radio"/> 0 <input type="radio"/> 1	
3	4	5	<input type="radio"/> 0 <input type="radio"/> 1		3	5	9	<input type="radio"/> 0 <input type="radio"/> 1	
4	2	6	<input type="radio"/> 0 <input type="radio"/> 1		4	4	9	<input type="radio"/> 0 <input type="radio"/> 1	
5	8	10	<input type="radio"/> 0 <input type="radio"/> 1		5	3	7	<input type="radio"/> 0 <input type="radio"/> 1	
6	6	14	<input type="radio"/> 0 <input type="radio"/> 1		6	1	4	<input type="radio"/> 0 <input type="radio"/> 1	
7	5	11	<input type="radio"/> 0 <input type="radio"/> 1		7	8	9	<input type="radio"/> 0 <input type="radio"/> 1	
8	3	8	<input type="radio"/> 0 <input type="radio"/> 1		8	6	14	<input type="radio"/> 0 <input type="radio"/> 1	
9	4	7	<input type="radio"/> 0 <input type="radio"/> 1		9	9	15	<input type="radio"/> 0 <input type="radio"/> 1	
10	9	13	<input type="radio"/> 0 <input type="radio"/> 1		10	2	11	<input type="radio"/> 0 <input type="radio"/> 1	
11	7	10	<input type="radio"/> 0 <input type="radio"/> 1		11	9	11	<input type="radio"/> 0 <input type="radio"/> 1	
12	3	4	<input type="radio"/> 0 <input type="radio"/> 1		12	8	17	<input type="radio"/> 0 <input type="radio"/> 1	
13	6	9	<input type="radio"/> 0 <input type="radio"/> 1		13	6	14	<input type="radio"/> 0 <input type="radio"/> 1	
14	8	14	<input type="radio"/> 0 <input type="radio"/> 1		14	1	7	<input type="radio"/> 0 <input type="radio"/> 1	
15	2	10	<input type="radio"/> 0 <input type="radio"/> 1		15	3	4	<input type="radio"/> 0 <input type="radio"/> 1	
16	5	7	<input type="radio"/> 0 <input type="radio"/> 1		16	4	7	<input type="radio"/> 0 <input type="radio"/> 1	
17	1	6	<input type="radio"/> 0 <input type="radio"/> 1		17	5	9	<input type="radio"/> 0 <input type="radio"/> 1	
18	8	9	<input type="radio"/> 0 <input type="radio"/> 1		18	2	7	<input type="radio"/> 0 <input type="radio"/> 1	
19	6	14	<input type="radio"/> 0 <input type="radio"/> 1		19	1	3	<input type="radio"/> 0 <input type="radio"/> 1	
20	9	15	<input type="radio"/> 0 <input type="radio"/> 1		20	9	10	<input type="radio"/> 0 <input type="radio"/> 1	
21	2	11	<input type="radio"/> 0 <input type="radio"/> 1		21	4	13	<input type="radio"/> 0 <input type="radio"/> 1	
22	4	6	<input type="radio"/> 0 <input type="radio"/> 1		22	5	9	<input type="radio"/> 0 <input type="radio"/> 1	
23	3	7	<input type="radio"/> 0 <input type="radio"/> 1		23	6	11	<input type="radio"/> 0 <input type="radio"/> 1	
24	5	8	<input type="radio"/> 0 <input type="radio"/> 1		24	2	8	<input type="radio"/> 0 <input type="radio"/> 1	
25	6	11	<input type="radio"/> 0 <input type="radio"/> 1		25	3	5	<input type="radio"/> 0 <input type="radio"/> 1	
26	5	11	<input type="radio"/> 0 <input type="radio"/> 1		26	8	11	<input type="radio"/> 0 <input type="radio"/> 1	
27	8	13	<input type="radio"/> 0 <input type="radio"/> 1		27	4	12	<input type="radio"/> 0 <input type="radio"/> 1	
28	9	17	<input type="radio"/> 0 <input type="radio"/> 1		28	2	6	<input type="radio"/> 0 <input type="radio"/> 1	
29	4	13	<input type="radio"/> 0 <input type="radio"/> 1		29	1	3	<input type="radio"/> 0 <input type="radio"/> 1	
30	3	7	<input type="radio"/> 0 <input type="radio"/> 1		30	9	10	<input type="radio"/> 0 <input type="radio"/> 1	
31	1	4	<input type="radio"/> 0 <input type="radio"/> 1		31	8	17	<input type="radio"/> 0 <input type="radio"/> 1	
32	2	3	<input type="radio"/> 0 <input type="radio"/> 1		32	3	11	<input type="radio"/> 0 <input type="radio"/> 1	
33	6	8	<input type="radio"/> 0 <input type="radio"/> 1		33	5	8	<input type="radio"/> 0 <input type="radio"/> 1	
34	3	9	<input type="radio"/> 0 <input type="radio"/> 1		34	6	11	<input type="radio"/> 0 <input type="radio"/> 1	
35	4	7	<input type="radio"/> 0 <input type="radio"/> 1		35	9	15	<input type="radio"/> 0 <input type="radio"/> 1	
36	8	12	<input type="radio"/> 0 <input type="radio"/> 1		36	8	17	<input type="radio"/> 0 <input type="radio"/> 1	
37	9	17	<input type="radio"/> 0 <input type="radio"/> 1		37	4	12	<input type="radio"/> 0 <input type="radio"/> 1	
38	5	14	<input type="radio"/> 0 <input type="radio"/> 1		38	3	7	<input type="radio"/> 0 <input type="radio"/> 1	
39	1	6	<input type="radio"/> 0 <input type="radio"/> 1		39	2	5	<input type="radio"/> 0 <input type="radio"/> 1	
40	2	3	<input type="radio"/> 0 <input type="radio"/> 1		40	5	7	<input type="radio"/> 0 <input type="radio"/> 1	
41	8	10	<input type="radio"/> 0 <input type="radio"/> 1		41	1	6	<input type="radio"/> 0 <input type="radio"/> 1	
42	1	9	<input type="radio"/> 0 <input type="radio"/> 1		42	6	7	<input type="radio"/> 0 <input type="radio"/> 1	
43	2	3	<input type="radio"/> 0 <input type="radio"/> 1		43	1	7	<input type="radio"/> 0 <input type="radio"/> 1	
44	5	7	<input type="radio"/> 0 <input type="radio"/> 1		44	8	9	<input type="radio"/> 0 <input type="radio"/> 1	
45	3	8	<input type="radio"/> 0 <input type="radio"/> 1		45	5	13	<input type="radio"/> 0 <input type="radio"/> 1	
46	9	12	<input type="radio"/> 0 <input type="radio"/> 1		46	6	11	<input type="radio"/> 0 <input type="radio"/> 1	
47	6	15	<input type="radio"/> 0 <input type="radio"/> 1		47	3	9	<input type="radio"/> 0 <input type="radio"/> 1	
48	4	10	<input type="radio"/> 0 <input type="radio"/> 1		48	2	5	<input type="radio"/> 0 <input type="radio"/> 1	
49	3	7	<input type="radio"/> 0 <input type="radio"/> 1		49	9	11	<input type="radio"/> 0 <input type="radio"/> 1	
50	6	9	<input type="radio"/> 0 <input type="radio"/> 1		50	4	13	<input type="radio"/> 0 <input type="radio"/> 1	

COMPLETED? YES NO TERMINATED REFUSED

DO NOT MARK
IN THIS
SHADED AREA

	SERIES 3 ISI - 16 Sec.	CORRECT RESPONSE	PARTICIPANT'S RESPONSE	0 = WRONG 1 = RIGHT	SCORES
1	4	-		0	0
2	8	12		0	0
3	6	14		0	0
4	2	8		0	0
5	2	4		0	0
6	9	11		0	0
7	3	12		0	0
8	4	7		0	0
9	5	9		0	0
10	8	13		0	0
11	1	9		0	0
12	6	7		0	0
13	3	9		0	0
14	8	11		0	0
15	6	14		0	0
16	2	8		0	0
17	4	6		0	0
18	1	5		0	0
19	9	10		0	0
20	5	14		0	0
21	1	6		0	0
22	9	10		0	0
23	8	17		0	0
24	2	10		0	0
25	5	7		0	0
26	4	9		0	0
27	6	10		0	0
28	3	9		0	0
29	6	9		0	0
30	3	9		0	0
31	2	5		0	0
32	9	11		0	0
33	1	10		0	0
34	8	9		0	0
35	5	13		0	0
36	4	9		0	0
37	9	13		0	0
38	6	15		0	0
39	2	8		0	0
40	4	6		0	0
41	3	7		0	0
42	5	8		0	0
43	8	13		0	0
44	1	9		0	0
45	5	6		0	0
46	6	11		0	0
47	9	15		0	0
48	8	17		0	0
49	3	11		0	0
50	1	4		0	0

	SERIES 4 ISI - 12 Sec.	CORRECT RESPONSE	PARTICIPANT'S RESPONSE	0 = WRONG 1 = RIGHT	SCORES
1	3	-		0	0
2	2	5		0	0
3	6	8		0	0
4	5	11		0	0
5	4	9		0	0
6	3	7		0	0
7	1	4		0	0
8	6	7		0	0
9	5	11		0	0
10	9	14		0	0
11	8	17		0	0
12	4	12		0	0
13	2	6		0	0
14	1	3		0	0
15	2	3		0	0
16	4	6		0	0
17	9	13		0	0
18	3	12		0	0
19	6	9		0	0
20	8	14		0	0
21	5	13		0	0
22	4	9		0	0
23	3	7		0	0
24	11	11		0	0
25	2	10		0	0
26	5	7		0	0
27	1	6		0	0
28	6	7		0	0
29	9	15		0	0
30	4	13		0	0
31	8	12		0	0
32	5	13		0	0
33	9	14		0	0
34	2	11		0	0
35	6	8		0	0
36	1	7		0	0
37	3	4		0	0
38	4	7		0	0
39	2	6		0	0
40	3	5		0	0
41	9	12		0	0
42	5	14		0	0
43	6	11		0	0
44	8	14		0	0
45	1	9		0	0
46	6	7		0	0
47	4	10		0	0
48	9	13		0	0
49	2	11		0	0
50	3	5		0	0

11. WISCONSIN CARD SORT

12) Wisconsin Card Sorting Test: This test is designed to assess concept formation, problem solving, and the use of feedback. The score used is the number of cards (out of 128) that a subject used in order to make 6 categorical sorts based on the examiners feedback.

WISCONSIN CARD SORTING TEST

PARTICIPANT NUMBER	TEST DATE			TEST NO	TESTER CODE	SCORER CODE
	MONTH	DAY	YEAR			
	01	02	03	04	05	06
	04	05	06	07	08	09
	09	10	11	12	13	14
	17	18	19	20	21	22
	23	24	25	26	27	28
	29	30	31	32	33	34
	35	36	37	38	39	40
	41	42	43	44	45	46
	47	48	49	50	51	52
	53	54	55	56	57	58
	59	60	61	62	63	64
	65	66	67	68	69	70
	71	72	73	74	75	76
	77	78	79	80	81	82
	83	84	85	86	87	88
	89	90	91	92	93	94
	95	96	97	98	99	00

PARTICIPANT NAME _____

REMARKS
COLOR BLIND YES NO

SORTS: C, F, N, C, F, N

1	C	F	N	C	F	N	23	C	F	N	C	F	N	43	C	F	N	C	F	N	63	C	F	N	C	F	N	83	C	F	N	C	F	N	103	C	F	N	C	F	N
2	C	F	N	C	F	N	24	C	F	N	C	F	N	44	C	F	N	C	F	N	64	C	F	N	C	F	N	84	C	F	N	C	F	N	104	C	F	N	C	F	N
3	C	F	N	C	F	N	25	C	F	N	C	F	N	45	C	F	N	C	F	N	65	C	F	N	C	F	N	85	C	F	N	C	F	N	105	C	F	N	C	F	N
4	C	F	N	C	F	N	26	C	F	N	C	F	N	46	C	F	N	C	F	N	66	C	F	N	C	F	N	86	C	F	N	C	F	N	106	C	F	N	C	F	N
5	C	F	N	C	F	N	27	C	F	N	C	F	N	47	C	F	N	C	F	N	67	C	F	N	C	F	N	87	C	F	N	C	F	N	107	C	F	N	C	F	N
6	C	F	N	C	F	N	28	C	F	N	C	F	N	48	C	F	N	C	F	N	68	C	F	N	C	F	N	88	C	F	N	C	F	N	108	C	F	N	C	F	N
7	C	F	N	C	F	N	29	C	F	N	C	F	N	49	C	F	N	C	F	N	69	C	F	N	C	F	N	89	C	F	N	C	F	N	109	C	F	N	C	F	N
8	C	F	N	C	F	N	30	C	F	N	C	F	N	50	C	F	N	C	F	N	70	C	F	N	C	F	N	90	C	F	N	C	F	N	110	C	F	N	C	F	N
9	C	F	N	C	F	N	31	C	F	N	C	F	N	51	C	F	N	C	F	N	71	C	F	N	C	F	N	91	C	F	N	C	F	N	111	C	F	N	C	F	N
10	C	F	N	C	F	N	32	C	F	N	C	F	N	52	C	F	N	C	F	N	72	C	F	N	C	F	N	92	C	F	N	C	F	N	112	C	F	N	C	F	N
11	C	F	N	C	F	N	33	C	F	N	C	F	N	53	C	F	N	C	F	N	73	C	F	N	C	F	N	93	C	F	N	C	F	N	113	C	F	N	C	F	N
12	C	F	N	C	F	N	34	C	F	N	C	F	N	54	C	F	N	C	F	N	74	C	F	N	C	F	N	94	C	F	N	C	F	N	114	C	F	N	C	F	N
13	C	F	N	C	F	N	35	C	F	N	C	F	N	55	C	F	N	C	F	N	75	C	F	N	C	F	N	95	C	F	N	C	F	N	115	C	F	N	C	F	N
14	C	F	N	C	F	N	36	C	F	N	C	F	N	56	C	F	N	C	F	N	76	C	F	N	C	F	N	96	C	F	N	C	F	N	116	C	F	N	C	F	N
15	C	F	N	C	F	N	37	C	F	N	C	F	N	57	C	F	N	C	F	N	77	C	F	N	C	F	N	97	C	F	N	C	F	N	117	C	F	N	C	F	N
16	C	F	N	C	F	N	38	C	F	N	C	F	N	58	C	F	N	C	F	N	78	C	F	N	C	F	N	98	C	F	N	C	F	N	118	C	F	N	C	F	N
17	C	F	N	C	F	N	39	C	F	N	C	F	N	59	C	F	N	C	F	N	79	C	F	N	C	F	N	99	C	F	N	C	F	N	119	C	F	N	C	F	N
18	C	F	N	C	F	N	40	C	F	N	C	F	N	60	C	F	N	C	F	N	80	C	F	N	C	F	N	100	C	F	N	C	F	N	120	C	F	N	C	F	N
19	C	F	N	C	F	N	41	C	F	N	C	F	N	61	C	F	N	C	F	N	81	C	F	N	C	F	N	101	C	F	N	C	F	N	121	C	F	N	C	F	N
20	C	F	N	C	F	N	42	C	F	N	C	F	N	62	C	F	N	C	F	N	82	C	F	N	C	F	N	102	C	F	N	C	F	N	122	C	F	N	C	F	N
21	C	F	N	C	F	N	43	C	F	N	C	F	N	63	C	F	N	C	F	N	83	C	F	N	C	F	N	103	C	F	N	C	F	N	123	C	F	N	C	F	N
22	C	F	N	C	F	N	44	C	F	N	C	F	N	64	C	F	N	C	F	N	84	C	F	N	C	F	N	104	C	F	N	C	F	N	124	C	F	N	C	F	N
							45	C	F	N	C	F	N	65	C	F	N	C	F	N	85	C	F	N	C	F	N	105	C	F	N	C	F	N	125	C	F	N	C	F	N
							46	C	F	N	C	F	N								86	C	F	N	C	F	N	106	C	F	N	C	F	N	126	C	F	N	C	F	N
							47	C	F	N	C	F	N														107	C	F	N	C	F	N	127	C	F	N	C	F	N	
							48	C	F	N	C	F	N																				128	C	F	N	C	F	N		

NO CARDS USED	NO CORRECT	NO STOPS	NO PERSEV RESPONSE	NO PERSEV ERRORS	CATEGORIES
0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0
1 1 1	1 1 1	1 1 1	1 1 1	1 1 1	1
2 2	2 2	2 2	2 2	2 2	2
3 3	3 3	3 3	3 3	3 3	3
4 4	4 4	4 4	4 4	4 4	4
5 5	5 5	5 5	5 5	5 5	5
6 6	6 6	6 6	6 6	6 6	6
7 7	7 7	7 7	7 7	7 7	7
8 8	8 8	8 8	8 8	8 8	8
9 9	9 9	9 9	9 9	9 9	9

COMPLETED? YES NO TERMINATED REFUSED

14 GROOVED PEGBOARD

14 and 15) Grooved Pegboard, Right Hand, Left Hand: This test is designed to assess manual dexterity and fine motor speed in each of the hands. Each hand is required to place a set of pegs into a grooved hole as quickly as possible. Their score is the number of seconds it takes them to complete the entire pegboard.

identical. Goldberg and Smith's criteria for each 60 second condition is simply two times the 30 second criterion for that condition. Performances are considered indicative of brain damage when one or more score below criterion occurs on both the first and the second trial for one or more 30 second conditions, or occurs on the 60 second trial for one condition. A 60 second score achieved by the nonpreferred hand that exceeds the preferred hand's score by three or more points indicates a lesion contralateral to the preferred hand. A 30 second score for the preferred hand that exceeds the 30 second score of the nonpreferred hand by five or more points suggests that the lesion is ipsilateral to the preferred hand.

Like many other useful neuropsychological instruments, the Purdue Pegboard Test varies greatly in the efficiency with which it identifies brain impairment. T. E. Goldberg and A. Smith (1976) report that, using their norms based on two trials for each condition, this test identified 80% (10% false positive, 10% false negative) of a large group of normal subjects and neurological patients correctly. Also using these norms, Berker and his colleagues (1982) found that in a group of 228 diagnostically mixed brain damaged persons, a larger number had motor than sensory deficits (using the Face-Hand Sensory Test, see p. 378), although both kinds of deficits are usually present with lateralized lesions. However, Heaton and his co-workers (1978) report that the proportion of correct differentiations between organic and various groups of psychiatric patients made by this test alone ranges from 76% to 46%. These are not very good odds on which to attempt a screening program.

GROOVED PEGBOARD (Kløve, 1963; Matthews and Kløve, 1964)

This test adds a dimension of complex coordination to the pegboard task. It consists of a small board containing a 5×5 set of slotted holes angled in different directions. Each peg has a ridge along one side requiring it to be rotated into position for correct insertion. It is part of the Wisconsin Neuropsychological Test Battery (Harley et al., 1980; Matthews and Kløve, 1964) and the Lafayette Clinic Repeatable Neuropsychological Test Battery (R. Lewis and Kupke, 1977) (see p. 566). Its complexity makes it a highly sensitive instrument for studying improvement in motor functions following stroke (Meier, 1974) and hemispheric components of motor performance (Haaland et al., 1977; Haaland and Delaney, 1981).

Time to completion is scored. Data have been handled in a variety of ways. Matthews and Haaland (1979) give the mean time averaged for both hands in a small ($n = 16$) group of mostly middle-aged (55 ± 5) control subjects as 35 seconds. One group of 14-year-old boys and girls performed the task in 66.5 ± 13.3 seconds using their preferred hands and 70.1 ± 7.5 seconds with the nonpreferred hand (Knights and Moule, 1968). Another group of 14 year olds, all male, took longer and showed much greater variability, performing the task in 78 ± 40.5 seconds with the preferred hand and in 81 ± 23.8 seconds with the nonpreferred hand (Trites, no date). R. Lewis and Kupke (1977) report that average scores for the preferred hand only were in the range of 71-79.5 seconds for epileptic patients under different drug conditions.

Grooved Pegboard

(label)

EXAM CODE /G/R/Q/1/ (0001-0004)

Participant ID /_/_/_/_/_/_/_/_/ (0005-0011)

Participant Name

Date Month /_/_/ (0012-0013)

Day /_/_/ (0014-0015)

Year /_/_/ (0016-0017)

Time Started Hour /_/_/ (0018-0019)

Min /_/_/ (0020-0021)

Interviewer ID /_/_/_/_/_/ (0022-0025)

Supervisor ID /_/_/_/_/_/ (0026-0029)

1. For most of your daily tasks, do you prefer to use your right hand, your left hand, or do you use either hand? /_/ (0030)

- 1 = right hand
- 2 = left hand
- 3 = either hand

- 8 = don't know
- 9 = refused

2. When you were a young child, did you prefer to use your right hand, your left hand, or did you use either hand?

/_/_/

(0031)

- 1 = right hand
- 2 = left hand
- 3 = either hand

- 8 = don't know
- 9 = refused

3. First Hand Tested

/_/_/

(0032)

- 1 = right hand
- 2 = left hand

- 7 = not applicable
- 8 = don't know
- 9 = refused

Note: TEST THE RIGHT HAND FIRST, IF THERE IS NO HAND PREFERENCE

EXPLAIN IN THE COMMENT SECTION IF THE PREFERRED HAND IS NOT TESTED FIRST

4. Completion time / First hand

minutes

/_/_/

(0033-0034)

seconds

/_/_/

(0035-0036)

- 97 = not applicable
- 98 = don't know
- 99 = refused

5. No. of pegs dropped / First hand

/_/_/

(0037-0038)

- 97 = not applicable
- 98 = don't know
- 99 = refused

6. Completion time / Second hand

minutes	___/___/	(0039-0040)
seconds	___/___/	(0041-0042)

97 = not applicable
98 = don't know
99 = refused

7. No. of pegs dropped / Second hand

___/___/ (0043-0044)

97 = not applicable
98 = don't know
99 = refused

8. Comment

_____ (0045-0088)

DESCRIBE ANY UNUSUAL FINDINGS THAT COULD INFLUENCE THIS TEST (E.G.,
NON-DOMINANT HAND TESTED FIRST, INTERFERRING NOISE, DID NOT UNDERSTAND
DIRECTIONS, ETC.

13 HANDEDNESS

16) Handedness Laterality Rating: This score represents the subject's handedness index as assessed by the Edinburgh Handedness Inventory. A score of 1.00 represents a 'pure' right hander, while a 0.00 is someone who reports only left hand use.

Please indicate your preference in the use of hands in the following activities by putting a check (✓) in the appropriate column.

Some of the activities require both hands. In these cases, the part of the task or object for which hand preference is wanted is clearly indicated.

Please try to answer all of the questions, and only leave a blank if you have no experience at all of the object or task.

	Always Left	Usually Left	Either Hand	Usually Right	Always Right
1. Writing					
2. Drawing					
3. Throwing					
4. Scissors					
5. Toothbrush					
6. Knife (without fork)					
7. Spoon					
8. Top hand when holding the handle of a shovel.					
9. Striking a match					
10. Twisting off the lid of a jar					
This space for department use only					
TOTALS	(2)	(1)	(0)	(1)	(2)

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Test Date _____ Debriefed _____ Test No. _____ Scorer No. _____

A Computer-Administered Neurobehavioral Evaluation System for Occupational and Environmental Epidemiology

Rationale, Methodology, and Pilot Study Results

Edward L. Baker, M.D., M.P.H.; Richard Letz, Ph.D.; and Anne Fidler, M.Sc.

To facilitate the conduct of epidemiologic studies of populations at risk for or suffering from central nervous system (CNS) dysfunction due to environmental agents, a computer-administered neurobehavioral evaluation system has been developed. The system includes a set of testing programs designed to run on a microcomputer and questionnaires to facilitate interpretation of results. Standard tasks evaluating memory, psychomotor function, verbal ability, visuospatial ability, and mood were selected and adapted for computer presentation following the recommendation of an expert committee of the World Health Organization and the National Institute for Occupational Safety and Health. In two pilot surveys, test performance was found to be influenced by age, education level, and socioeconomic status in ways consistent with prior research findings. Performance on tests of short-term memory and reaction time was negatively correlated with intensity of organic solvent exposure among industrial painters. In view of the ease of administration and data handling, high subject acceptability, and sensitivity to the effects of known neurotoxic agents, computer-based assessment of CNS function holds promise for future epidemiologic research.

Neurobehavioral tests have been used widely to evaluate cognitive function following human exposure to

neurotoxic agents.¹ These studies have shown a variety of adverse effects on the central nervous system (CNS) that have been reviewed in detail elsewhere.^{2,3} Although somewhat similar techniques were used in many of these studies, significant variability in testing procedures between studies unfortunately has made comparison of results difficult. Furthermore, the procedures used require extensive interviewer involvement, with attendant error due to variation in testing procedures. Such error impairs the ability of the study to detect subtle health effects.⁴ Additionally, systematic error introduced by interviewer bias may further distort study results.

An additional concern exists regarding the intelligibility of the results of past studies. Since a wide variety of tests have been used in past investigations, health professionals lacking formal training in psychology or a related discipline have great difficulty in interpreting study findings. Also, because neurobehavioral epidemiology is being used with increasing frequency to establish standards of occupational and environmental exposures to neurotoxic agents, intelligibility of test results is an important consideration for standard setting. Finally, the variability in test procedures among studies precludes the pooling of data on unexposed individuals in an attempt to explore the effects of extraneous factors (e.g., age, education level, and sex) on test performance. Clearly, our ability to use these tests to evaluate exposed populations is dependent on our understanding of the determinants of test performance in unexposed groups.

In a recent review of neurobehavioral studies of populations exposed to organic solvents, Cherry and Waldron⁵ indicated that prospective evaluations of working populations hold particular promise for future epidemiologic

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work. We concur in this assessment of the need for prospective studies and feel that, in this context, tests with maximum reproducibility are needed. For this and other reasons, we have adapted certain tests of neurobehavioral function to a computer-administered format.

In choosing tests for inclusion in our set, we have reviewed the previous literature in which test sets for use in epidemiologic investigations have been specified. An extensive set is that developed at the Finnish Institute of Occupational Health.⁶ More recently, an expert committee convened by the World Health Organization (WHO) and the National Institute for Occupational Safety and Health (NIOSH) proposed a core set of neurobehavioral tests for use in occupational epidemiologic studies and a list of supplemental tests suitable for certain situations.⁷ This is the only core set developed by an international group with specific experience in epidemiologic study of occupational groups. Clearly, the process of specifying a test set is an evolving one that will be facilitated by further experience. For our current choice of tests to adapt for computer administration, we were guided significantly by the views of the WHO-NIOSH group, as well as by our prior experience.⁸

The tasks that we have chosen include ones adapted from clinical neuropsychology that have also been used widely in prior field studies of workplace neurotoxic agents. As a result, most of our tests are recognizable to practitioners in the field since they are adaptations of preexisting instruments. In selecting our set of tests, we were guided primarily by clinical and epidemiologic experiences rather than theoretical considerations from the field of cognitive psychology. We feel strongly that there is an important role for other sets of tests that derive directly from current psychological theory (e.g., Foree et al⁹) in evaluating populations exposed to environmental neurotoxic agents. Such tests will prove particularly useful in exploring mechanisms of neurotoxin action and will undoubtedly be found to be useful in combination with other techniques for evaluating CNS function.

The testing system described herein is designed for use in epidemiologic field studies of human populations exposed to neurotoxic agents in the workplace or the general environment. Our approach offers techniques that can be administered on portable equipment by technicians with minimal training. The tests chosen evaluate a broad range of CNS functions, including psychomotor function, memory, visuospatial ability, verbal ability, and mood. We have not selected tests of sensory function, which should be included in most evaluations of populations exposed to workplace or environmental neurotoxic hazards. Further development of such tests is needed. We do not feel that the current set of tests should be considered as a fixed battery to be used in all situations. Rather, a more appropriate approach is one in which tests are selected from those noted for use in specific circumstances.

Computer-administered behavioral testing techniques offer certain advantages and disadvantages that should be carefully considered prior to their use. The primary advantages of a computer-administered system include the reproducibility of testing conditions, ease of data hand-

ling, ease of scoring, and immediate reporting of results to individuals participating in the testing session. Immediate feedback of test results, if properly performed, improves the level of motivation of persons being tested. Furthermore, the use of a computer alters the dynamics of the testing situation in a way that provides a nonthreatening challenge to the individual, which thereby encourages participation.

Some disadvantages of computer-administered system are the cost and availability of equipment as well as the unusual quality of the interaction between the person being tested and the computer itself. Although many persons in the past were quite unfamiliar with the use of computers, this situation is rapidly changing with the proliferation of home computers, computerized banking machines, and video games. Therefore, interacting with a computer is not as unusual in developed countries today as it was a few years ago. Since the computer systems being considered for this application may also be used for other applications by scientific groups, including the analysis of data from surveys and word processing, the costs of obtaining a computer system for neurobehavioral testing can be justified for other reasons. Furthermore, with the advent of powerful, affordable systems, the versatility of the available hardware has made field testing using these units quite feasible. Although the use of computers does increase somewhat the complexity of the testing situation, some existing tests included in the WHO core test battery and supplementary tests⁷ do require electronic equipment for their performance. Therefore, it appears that a place exists for the use of computer-administered neurobehavioral tests in the monitoring and study of populations exposed to neurotoxic agents. Such a battery has been field tested by our group and found useful in field studies of several population groups.

Rationale for Test Selection

Our automated neurobehavioral evaluation system currently includes 12 separate tasks (Table 1); others are under development. All tests listed have been successfully administered in field surveys of working populations.

Five of the tests (Table) are modifications of tests within the seven-test WHO core battery.⁷ The two other tests in the WHO core battery do not lend themselves to computer administration. In addition, we have implemented programs for the verbal paired-associate learning and the continuous performance tests that were specified as suitable supplements to the WHO core set. The Sternberg memory-scanning test and the vocabulary test were adapted from existing tests, not listed by the WHO committee, to evaluate memory and verbal ability. The pattern recognition and pattern memory tests are similar to existing computer-administered screening tests.¹⁰ Only one totally new test, the hand-eye coordination task, was developed for inclusion in the set. Further discussion of the rationale and process of test selection is provided in previous publications.^{8,11-14}

Description of Individual Tests and Rationale for Their Selection

Psychomotor Performance—1. Symbol-Digit Substitution Test—This task is a modification of the Digit-Symbol Sub-

Computer-Administered Neurobehavioral Evaluation System		
Function	Test	Administration Time, min
Psychomotor performance		
Speed/coding ability	Symbol-digit*†	6
Dexterity	Hand-eye coordination†	4
Speed	Simple reaction time*†	5
Attention/speed	Continuous performance†‡	6
Memory		
Memory/attention	Digit span*†	10
Verbal memory (short-term and intermediate)	Paired-associate learning‡ (with delayed recall)	12 2
Visual memory	Visual retention*	10
Visual memory	Pattern memory†	5
Memory processing	Memory scanning†	8
Verbal		
Verbal ability	Vocabulary	10
Mood		
Mood	Mood scales*†	7
Visuospatial ability		
Cognitive ability	Pattern recognition†	5

* WHO core test

† Suitable for repeated measures design

‡ WHO supplemental test

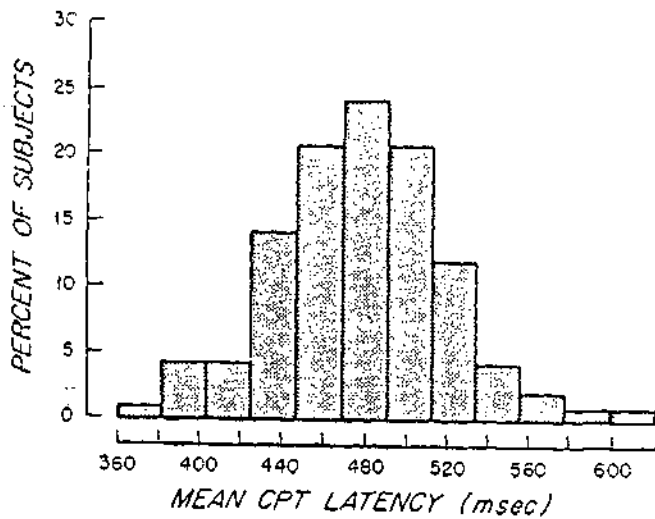


Fig. 1 — Distribution mean response latencies on continuous performance test of 68 unexposed bricklayers.

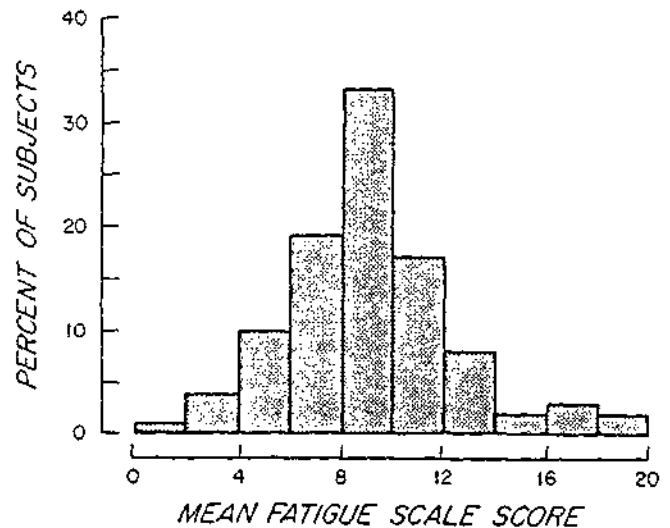


Fig. 2 — Distribution of scores of 68 unexposed bricklayers on fatigue scale from mood scale.

stitution test from the Wechsler Adult Intelligence Scale.¹⁵ A computerized version of the symbol-digit task has been found to be of value in automated screening of psychiatric patients.¹⁰ In addition to being included in the WHO core set,⁷ the Digit-Symbol test, which evaluates *speed* and *coding* ability, has been found useful in prior epidemiologic studies of individuals exposed to lead, carbon disulfide, and solvent mixtures.³ In our adaptation, nine symbols and digits are paired at the top of the screen and the subject has to press the digit keys corresponding to a reordered test set of the nine symbols. The time required to complete each symbol-digit set and the number of digits incorrectly matched are recorded. Four sets of nine symbol-digit pairs are presented in succession. The pair-

ing of symbols with digits is varied between sets to avoid learning.

2. *Hand-Eye Coordination Test*—The individual is asked to use a joystick to trace over a large sine wave pattern on the video display terminal. A cursor moves horizontally at a constant rate, while the individual controls only the vertical motion of the cursor with the joystick. Deviations from a set line (mean absolute error and root mean square error) are recorded and constitute measures of coordination ability. This task evaluates *dexterity*, a function found to be disrupted in previous studies of various neurotoxic agents.^{2,11,16}

3. *Simple Reaction Time*—In this test, the individual is

asked to press a button when seeing a large "0" on the screen. The interstimulus interval is varied randomly between 2.5 and 7.5 s to reduce anticipation effects. Data are recorded as individual reaction times over the presentation of 60 stimuli and the response latencies are averaged over blocks of 12 trials. Reaction time testing has been a widely used technique for monitoring exposed workers.¹⁷

4. *Continuous Performance Test (CPT)*—This test measures sustained visual attention by having the subject press a button upon seeing a large letter "S" when it is projected onto a video display terminal.¹⁸ A series of letters, 20% of which are the letter "S," flash briefly (for about 50 ms) on the screen at a rate of one per second for five minutes. Recording and storage of individual response latencies allow for computation of mean reaction time, learning effects noted during the early stage of the task, and variability in attention that occurs during the latter part of the test. Omission and commission errors are also recorded. Previous research has utilized this form of testing extensively in evaluating solvent^{16,17} and lead neurotoxicity.¹⁹ A report of CPT results can be graphically displayed to the subject at the end of the entire testing session.

Memory—1. *Digit Span*—This widely used clinical test is a part of the Wechsler Adult Intelligence Scale²⁰ and Wechsler Memory Scale.²⁰ The individual must enter into the computer progressively longer series of digits following visual presentation at a rate of one per second by the computer. After incorrectly responding to two trials at a span length, the task changes such that the individual must enter a new digit series in reverse order. Previous studies of solvent and lead toxicity have utilized this test as a measure of short-term memory and attention.^{2,11,21}

2. *Paired-Associated Learning Test (With Delayed Recall)*—In a standard task²⁰ of short-term verbal memory, word pairs are read from the visual display screen by the interviewer at a rate controlled by the computer. The acceptable response time is also computer controlled. The series of words is presented three times with varying internal order, and scores, consisting of the number of correct associations, are given for each trial. An additional trial containing the same words is given at the end of the testing session, following a delay of more than 30 minutes, as a test of memory encoding and intermediate recall. This is the only task within our set requiring direct interviewer participation.

3. *Visual Retention Test*—The Benton test of visual memory is administered in many standard neuropsychological batteries.²² We have developed a similar approach in which the machine presents the test figure(s) followed by four similar figures from which the individual must select the figure(s) previously seen. The computer records the number correct and the response times for correct and incorrect responses.

4. *Pattern Memory Test*—In this task, a pattern consisting of several geometric figures formed by small blocks is presented for a brief period. The pattern is then removed and replaced by three similar patterns, one of which is identical to the original stimulus. The task is repeated with different stimulus and choice patterns to a total of 15 trials.

Task difficulty may be increased by increasing the degree of correspondence of the incorrect patterns to the correct one. The computer records number of correct responses and latency time for correct and incorrect responses. Since the pattern composition is varied randomly, this test of visual memory is suitable for repeated administration. A similar task has been described previously.¹⁰

5. *Memory-Scanning Test*—The subject is shown a series of digits and must indicate whether a digit presented subsequently comes from a previously presented set.²² Responses are scored as correct/incorrect and response latencies are recorded. The set size of digits to be presented can be varied from two to five and regression techniques used to assess total cognitive encoding and motor processing time, difference in mean response time for positive and negative trials, and memory-scanning time. The computer program used to administer the tests is modified from that used by Smith and Langolf.²³ The test measures the actual processing time required to recall previously stored (i.e., learned) information and has been shown to be sensitive to chronic mercury exposure.²⁴

Verbal Abilities—1. *Vocabulary*—In our modification of a vocabulary subtest from the Armed Forces Qualifying Test,²⁵ 25 words are presented and the subject is asked to select, from a set of four words, the synonym for the presented word. This test is said to provide an index of stable CNS function.¹¹ In developing this test some new sets of words were created to increase task difficulty as discussed below under "Pilot Testing."

Mood—1. *Mood Scales*—This presentation modifies a self-administered questionnaire²⁴ in which subjects rate themselves with respect to their feelings during the previous seven days. This mood survey has been used successfully in the evaluation of the efficacy of psychotherapeutic drugs and in classifying individuals with various neurobehavioral disorders.²⁴ Our adaptation is limited to 25 items and yields a five-dimensional mood profile (tension, depression, anger, fatigue, and confusion) by combining ratings on individual items. Our prior studies of lead toxicity have shown that a mood survey is useful and sensitive in the evaluation of CNS effects of occupational lead exposure.¹⁹

Visuospatial Ability—1. *Pattern Recognition Test*—In this task, three patterns similar to those generated for the pattern memory task (described above) are presented on the screen at the same time. Two are identical. The task consists of identifying which of the three is different. Number of correct responses and individual response latencies are recorded. As with the pattern memory test, the method of generating the patterns is such that repeated trials can be performed. The test appears to evaluate the higher processes involved in the organization of visual material, i.e., visuospatial ability.¹¹ A similar task has been described.¹⁰

Computer Configuration

Hardware—The software used for test administration was developed using an IBM personal computer (PC). The speed and power of the 16-bit 8088 microprocessor allow millisecond accuracy while working in an interpreted language. A joystick as well as two push buttons provide input for cursor controls. Field testing in our offices and

in pilot projects utilized the IBM PC. More recent testing has utilized the COMPAQ Computer (COMPAQ Computer Corp., Houston), which is totally compatible with IBM software and hardware. Video display is performed through a built-in 9-in monitor. Use of this microcomputer permits testing with a portable, 28-lb test system. The programs run on some other IBM PC-compatible computers.

Software—The software that administers these tests is written in IBM's Advanced BASIC. Input/output statements and functions standard in this implementation of the language allow the flexibility of an interpreted language with great speed of graphic presentation. Separate files are developed for each subject, containing some identification data and the test results. Each test in the battery is individually administrable. Minimal training time is necessary for interviewers because they are given the option, through a screen menu, of choosing the tests and test order to be administered to each subject. A default option can provide a fixed set of tests established by the investigator. Timing of response latencies is accomplished by a software clock. Timing resolution is about 0.5 ms. Standard communications software permits data transfer over telephone or dedicated communication lines to larger computers for analysis using standard statistical software packages. A summary of test results can be displayed on the screen or printed out immediately after testing.

Mode of Presentation—After the procedures are briefly explained by a research technician, all additional instructions are read from the video screen. Instructions have been simplified to avoid complicated passages and ambiguous phrases. With the exception of the Paired-Associate Learning Task, little interaction occurs between the technician and the tested individual until the testing sequence is completed, unless assistance is needed in understanding the task. The computer is programmed to monitor inappropriate responses (e.g., holding down the joystick button too long or continuously failing to respond to appropriate stimuli) and to instruct the individual to modify his approach to the testing session. Practice trials are performed on certain tests to ensure that the tests are understood. Testing procedures are described below under pilot studies.

Pilot Testing

Background—Development of our system has occurred incrementally as programs were written, field tested, and evaluated for subsequent use. The two pilot studies were performed at a stage when only a portion of the current test set (Table) had been developed. The purposes of these studies were (1) to evaluate the portability and subject acceptability of our computer-based system, (2) to determine training requirements of interviewers and to clarify their role during testing, (3) to develop a strategy for evaluation and control of extraneous factors that might alter test performance, and (4) to examine the distribution and determinants of test performance in a working population unexposed to neurotoxic agents in their jobs.

Methods—Before coming to the test site, each person completed a detailed work-health questionnaire regarding prior health conditions, prior jobs and job-related chemical exposures, current and past habits (i.e., alcohol and

cigarette consumption history), and current symptoms; the questionnaire was reviewed for accuracy and completeness by an interviewer. Immediately before test administration, a pretest questionnaire designed to evaluate transient conditions (e.g., physical injuries, alcohol or drug consumption, sleep deprivation, and emotional trauma) was also administered. Those persons found to be acceptable for neurobehavioral testing were then provided brief instructions by an interviewer and left alone to proceed with the test series. The interviewer remained nearby to monitor the session and to be available if questions or problems arose. At the completion of the tasks, the interviewer displayed the subject's results on the continuous performance task (CPT) on the video display terminal. A written report of test results was provided with appropriate explanations several weeks later by mail.

Test Selection—Six tests were used from the system: the mood scales, CPT, hand-eye coordination, digit span, simple reaction time, and the vocabulary subtest from the Armed Forces Qualifying Test. The choice of tests was determined by an interest in evaluating mood, psychomotor ability, memory, and verbal ability and by the stage of development of our system.

Statistical Analysis—Simple frequency distributions of each variable were derived and histograms for selected tests were constructed. Multiple regression analyses designed to evaluate the impact of selected predictor variables on test performance were executed using a computer software package (Statistical Analysis System, Cary, N.C.) run on an IBM mainframe computer.

Unexposed Population Study

Procedure—In April, 1982, a group of union bricklayers was evaluated as part of a multiphasic health evaluation that included, in addition to neurobehavioral evaluation, pulmonary function testing, chest roentgenography, and other clinical tests. We excluded data for persons with evidence of acute alcohol or drug consumption, poor English comprehension ability, or incomplete information, leaving data for 68 individuals for analysis.

Results—The 68 bricklayers whose data were analyzed were typical of U.S. working males: they had a mean age of 47.8 years, with a mean of 11.6 years of schooling; their parents were of lower socioeconomic class using the scale of Hollingshead and Redlich²³ (class 4, out of five classes); they reported consumption of an average of 2.4 alcoholic drinks per day.

The distributions of raw scores on the six tests were generally Gaussian (Figs. 1 and 2). Log transformation of the scores of the hand-eye coordination test (root mean squared deviation from pattern line) was required to yield an approximately Gaussian distribution. A ceiling effect was observed with the Armed Forces Qualifying Test vocabulary test such that 25% of those tested had either zero or one error of the 25 items. We have subsequently modified our vocabulary test to address this problem.

Multiple regression analyses showed that performance on tests of psychomotor function (i.e., CPT, simple reaction time, and hand-eye coordination) consistently were negatively correlated with age, as anticipated from previous literature.^{10,11} Vocabulary test performance was pos-

itively correlated with number of years of schooling ($p = 0.03$); which was also consistent with prior research. Memory test results correlated best with number of years of education ($p = 0.09$ for digit span, backward). Alcohol consumption history (average number of drinks per occasion) did not show a clear pattern of association with test performance in this group.

Exposed Population Study

Procedures—In April, 1982, we evaluated another group of construction trade workers: industrial painters and dry-wall tapers. The painters were exposed to a variety of organic solvents that previous reports¹⁴ have indicated may affect neurobehavioral function both transiently and persistently. In contrast, dry-wall tapers, although exposed to asbestos in the past, have not been exposed to organic solvents or other workplace neurotoxic agents. Following exclusions for reasons described above for the other pilot study, 66 workers were available for analysis. In view of the small number of dry-wall tapers ($N=17$), their data were combined with those of the painters and used in a multiple regression analysis. In this analysis, two exposure terms were used to estimate the intensity of solvent exposure: the number of hours worked with paints during the past year and whether the individual had worked with paints during the past month. Both indices were derived from union records. We also asked individuals to recall their work experience, and their reports correlated well with union records ($r=0.75$). Other terms in the multiple regression model were age, number of years of education, and parental socioeconomic status (as measured by the Hollingshead Index). In view of the high correlation between number of years worked as a painter and age, we did not include this term in the model to avoid poor parameter estimation due to collinearity. Significance levels (two-tailed p values) for each coefficient were calculated using the t statistic.

Results—As observed in the bricklayers' pilot study, we noted associations between test performance and age and education level, as anticipated on the basis of previous reports¹²: older individuals demonstrated significantly worse performance on the continuous performance test ($p=0.005$), hand-eye coordination test ($p=0.0003$), and backward digit span ($p=0.02$); those with better education performed better on the vocabulary test ($p=0.0001$), forward digit span ($p=0.02$), and the continuous performance test ($p=0.05$); parental socioeconomic status showed modest correlations with test performance but of a magnitude that was less striking than those noted for age and schooling. As seen with the pilot study of bricklayers, chronic alcohol use was not found to be significantly associated with test performance.

Some associations were noted between the two measures of painting frequency and test performance. Recent heavy exposure to paints during the month prior to testing was associated with reduced forward digit span ($p=0.08$), whereas the amount worked during the past year was correlated with lower performance on simple reaction time ($p=0.05$).

Discussion

The computer-based neurobehavioral evaluation sys-

tem described herein offers several advantages over current conventional approaches, including a battery that we have recently described.⁶ Computer administration improves the reproducibility of test conditions and facilitates data handling and scoring. Portable computers are now available that permit the use of these systems in field locations. A minimum level of training is required for technicians who operate the system. Validation studies are now under way to compare our computer-administered tasks with conventional methods of test administration, to evaluate the reproducibility of the tests, and to assess the effect of alcohol consumption on test performance.

Our pilot studies demonstrated a high degree of acceptability of this portable computer-based system among blue-collar workers. The experience of using the computer was found to provide a nonthreatening, positively motivating format for evaluating neurobehavioral function. Minimal interviewer involvement was found to be necessary. Statistical analyses showed that test performance was correlated with age, education, and parental socioeconomic status in a fashion consistent with prior research findings. Exposure to solvents among industrial painters was associated with performance decrements on certain tests.

Despite the promise of this system, we are concerned about its potential misuse. The ease of test administration using the computer system could lead to widespread use by individuals unqualified in interpretation of test results. An even more significant concern, recently discussed in an editorial in *Science*,²⁶ is that the system will be used inappropriately to make decisions concerning employment status. Since cultural and demographic factors influence performance on tests such as ours, using these tests in an employment decision could discriminate against certain groups. For these reasons, we feel that the system should be limited to the use of trained medical professionals for application in a comprehensive program designed to prevent or treat disease or health impairment.

Our primary goal has been to provide tools for screening populations at risk for CNS dysfunction resulting from overexposure to neurotoxins in the workplace or the general environment. Clearly, other applications exist for the use of this system beyond our intended application, particularly in clinical medicine as a tool for evaluating the efficacy of treatment regimens and as a diagnostic aid. We feel that the development of computer-based systems such as ours will extend and enhance the capabilities of clinical neuropsychologists, as recently discussed,²⁷ and will provide an important tool for epidemiologists evaluating the effects of environmental neurotoxic agents.

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SOFT TISSUE SARCOMA

CLASSIFICATION

INTERNATIONAL HISTOLOGICAL CLASSIFICATION OF TUMOURS

No. 3

HISTOLOGICAL TYPING OF SOFT TISSUE TUMOURS

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for the Histological Definition and Classification of Soft Tissue Tumours*

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* From December 1958 until June 1960 the Head of the Centre was Dr D. J. Winslow.

PREFACE

Among the prerequisites for comparative studies of cancer are international agreement on histological criteria for the classification of cancer types and a standardized nomenclature. At present, pathologists use the same histological description for tumours of different primary sites, while conversely different terms are applied to the same pathological entity. An internationally agreed classification of tumours, acceptable alike to physicians, surgeons, radiologists, pathologists and statisticians, would enable cancer workers in all parts of the world to compare their findings and would facilitate collaboration among them.

In a report published in 1952,¹ a subcommittee of the WHO Expert Committee on Health Statistics discussed the general principles that should govern the statistical classification of tumours and agreed that, to ensure the necessary flexibility and ease in coding, three separate classifications were needed according to (1) anatomical site, (2) histological type, and (3) degree of malignancy. A classification according to anatomical site is available in the International Classification of Diseases, the foundations of which were laid as long ago as 1853 when the first international statistical congress was held in Brussels. Responsibility for the decennial revision of the international lists of causes of disease and death was taken over in 1924 by the Health Organisation of the League of Nations and since 1947 has passed to the World Health Organization. The 1965 revision² contains a much more detailed classification of neoplasms by anatomical site than its predecessors.

The question of establishing a universally accepted classification by histological type has received much attention during the last 20 years and a particularly valuable Atlas of Tumor Pathology—already numbering more than 30 volumes—is being published in the USA by the Armed Forces Institute of Pathology under the auspices of the National Research Council. An Illustrated Tumour Nomenclature in English, French, German, Latin, Russian and Spanish has also been published by the International Union Against Cancer (UICC).

¹ *World Hlth Org. techn. Rep. Ser.*, 1952, No. 33, p. 45.

² *World Health Organization (1967) Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death, 1965 revision, Geneva.*

The World Health Organization was brought into the picture in 1956 when the WHO Executive Board passed a resolution¹ requesting the Director-General to explore the possibility that WHO might organize centres in several places in the world and arrange for the collection of human tissues and their histological classification. The main purpose of such centres would be to develop histological definitions of cancer types and to facilitate the wide adoption of a uniform nomenclature. This resolution was endorsed by the Tenth World Health Assembly in May 1957² and the following month a Study Group on Histological Classification of Cancer Types met in Oslo to advise WHO on its implementation. The Group recommended criteria for selecting tumour sites for study and suggested a procedure for the drafting of histological classifications and their rigorous testing. Briefly, the procedure is as follows:

1. For each tumour site, a tentative histopathological typing and classification is drawn up by a group of experts, consisting of up to ten pathologists working in the field in question.

2. An international reference centre and a number of collaborating laboratories are then designated by WHO to evaluate the proposed classification. This is done by exchanging histological preparations in the form of microscope slides and paraffin blocks, accompanied by clinical histories and the histological typing in accordance with the proposed classification. Subsequently, one or more technical meetings are called by WHO to facilitate an exchange of opinions. If necessary, the classification is then amended to take account of criticisms.

3. The international reference centre then prepares sets of microscope slides covering all the proposed histological types and sends these with the revised classification to not more than ten independent pathologists for their comments and suggestions.

4. When replies have been received from all these reviewers, the classification is again revised in accordance with their comments. The international reference centre then prepares 100 sets of microscope slides of the various histological types and also drafts a text explaining the basis of the classification. In addition, photomicrographs are taken of the appropriate fields for the preparation of 35-mm transparencies and colour plates.

Since 1958, WHO has established 16 international reference centres covering tumours of the lung, breast, soft tissues, oropharynx, bone, ova-

ries, salivary glands, thyroid, skin, male urogenital tract, jaw, uterus, stomach and oesophagus, and intestines, as well as oral precancerous conditions and the leukaemias and lymphomas. This work involves at present 160 pathologists from 42 countries. It is planned to designate another 5 centres for tumours of the liver, eye, central nervous system, upper respiratory tract and endocrine glands. The International Reference Centres for Lung, Breast, Soft Tissues and Oropharyngeal Tumours have already completed their work, and the centres dealing with tumours of bones, salivary glands and jaws are expected to have their classifications ready in the near future.

The World Health Organization is deeply indebted to the many pathologists who have collaborated and are collaborating in this large undertaking, especially to the heads of the international reference centres and the collaborating laboratories. Grateful acknowledgement is also made to the many other international and national organizations whose pioneer work in the field of histological classification of tumours has greatly facilitated the task undertaken by WHO. Finally, WHO wishes to record its appreciation of the co-operation of the International Council of Societies of Pathology (ICSP), which has undertaken to distribute copies of the classifications, with corresponding sets of microscope slides, to national societies of pathology all over the world.

* * *

The WHO International Reference Centre for the Histological Definition and Classification of Soft Tissue Tumours was established in 1958 at the Armed Forces Institute of Pathology, Washington, D.C.

At a meeting in Geneva in 1959 attended by Dr B. J. P. Becker, Johannesburg; Dr J. Campos R. de C., Lima; Dr J. Clemmesen, Copenhagen; Dr R. Lattes, New York; Dr N. O. E. Ringertz, Stockholm; Dr C. Sirtori, Milan; Dr A. J. Strukov, Moscow; and Dr D. J. Winslow, Washington, D.C., a tentative classification of soft tissue tumours was drafted. This was then evaluated by the International Reference Centre and its Collaborating Centres, a list of which will be found on p. 5.

Subsequently, the International Reference Centre began to distribute material (clinical information and unstained slides) from selected cases of soft tissue tumours and related conditions to the five Collaborating Centres for histological typing according to the tentative classification. The histological and clinical material on soft tissue tumours available from the files of the Armed Forces Institute of Pathology, Washington, D.C., was

¹ *Off. Rec. Wld Hlth Org.*, 1956, 68, 14 (Resolution EB 17.R.40).

² *Off. Rec. Wld Hlth Org.*, 1957, 79, 467 (Resolution WHO 10.18).

extremely valuable in this work. A total of 520 tumour cases have been studied by the International Reference Centre and its Collaborating Centres. All the histological preparations from these cases were reviewed at meetings held in 1962 and 1965 and attended by the heads of the centres. At a final meeting in 1966, the tentative classification was adopted. This classification was then reviewed by ten pathologists who had been designated by WHO (see p. 5).

In the light of the criticisms and suggestions received, the Head of the International Reference Centre, assisted by Dr R. Lattes and Dr H. Torloni, prepared the final classification, together with explanatory notes and colour photomicrographs. The latter are reproduced as colour plates in the book and are also available as a collection of transparencies intended especially for teaching purposes.

In view of the large variety of soft tissue tumours and tumour-like lesions it was decided to group them in the following broad categories: fibrous tissue, adipose tissue, muscle tissue, blood vessels, lymph vessels, synovial tissue, mesothelial tissue, peripheral nerves, sympathetic ganglia, paraganglionic structures, pluripotential mesenchyme, embryonic structures, extragonadal germ cell origin, and disputed or uncertain histogenesis. An additional category comprising non-neoplastic and questionable neoplastic lesions of soft tissue has been included because of the resemblance of these lesions to true neoplasms.

It will, of course, be appreciated that the classification reflects the present state of knowledge and modifications are almost certain to be needed as experience accumulates. Furthermore, it necessarily represents a majority view, from which some pathologists may wish to dissent. It is nevertheless hoped that, in the interests of international co-operation, all pathologists will try to use the classification as put forward. Criticisms and suggestions for its improvement will be welcomed.

The World Health Organization is greatly indebted to Dr F. M. Enzinger, Head of the International Reference Centre, for his constant support and collaboration, and wishes also to thank the Director of the Armed Forces Institute of Pathology for making available the facilities needed for the work of the Centre. The assistance given by Dr R. Lattes is also gratefully acknowledged.

GENERAL GUIDE TO THE TYPING OF SOFT TISSUE TUMOURS

Although knowledge of soft tissue tumours has increased greatly in recent years, there is still much confusion concerning their incidence and behaviour and the best mode of therapy. This confusion is due not only to the wide morphological range and the relative rarity of soft tissue tumours but also to the lack of a standardized and widely accepted nomenclature and classification.

Terminology

For the purposes of this classification "soft tissues" are defined as including all non-epithelial extraskeletal tissues of the body with the exception of the reticuloendothelial system, the glia, and the supporting tissues of specific organs and viscera. The neuroectodermal tissues of the peripheral and autonomic nervous system are also included because the tumours of this group pose similar problems in diagnosis and treatment.

The terms "tumour" and "neoplasm" are used here to indicate "an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of normal tissue and persists in the same excessive manner after cessation of the stimuli which evoked the change" (R. A. Willis). A cellular proliferation the neoplastic nature of which is in doubt is designated as a "growth", "process", or "lesion". A decision as to the neoplastic or non-neoplastic nature of a given soft tissue growth is often exceedingly difficult, if not impossible.

The terms "malignant" and "sarcoma" are used throughout this classification to denote that the tumour is capable of metastasis. These terms, however, give little information as to the likelihood and speed of metastasis. Some malignant soft tissue tumours, such as the myxoid liposarcoma, metastasize only rarely and at a late stage of the disease, while others, such as the alveolar rhabdomyosarcoma, produce metastases—blood-borne and via the lymph stream—in virtually all cases and without much delay. These notable differences in the clinical course exist not only between neoplasms of different histogenetic type but also between morphologically different subvarieties of certain soft tissue tumours. Liposarcoma, for instance, shows such a wide range in its pattern and behaviour that the term liposarcoma alone without reference to its histological subtype is quite meaningless for prognosis and adequate therapy.

The terms "well differentiated" and "poorly differentiated" are used to indicate the relative maturity of the tumour cells as judged by their more or less pronounced resemblance to the cells of normal adult tissue. In most instances the degree of differentiation is a reliable index of the future clinical behaviour. But sometimes differentiation is misleading. Certain leiomyosarcomas, for example, may metastasize widely despite their relatively high degree of differentiation. Fibrosarcomas, on the other hand, when occurring in infants and small children, tend to pursue a less aggressive clinical course than one would expect from their immature histological appearance. Moreover, in evaluating the prognostic significance of the degree of differentiation it must be remembered that some soft tissue tumours display a fairly wide range in their morphological picture making it mandatory to examine several sections taken from various portions of the tumour whenever possible.

Principles of classification

In the preparation of this classification the attempt has been made to list all recorded and generally recognized primary neoplasms of soft tissues regardless of their relative incidence. Hamartomas and certain lesions of questionable neoplastic origin are included because of their importance for differential diagnosis and the difficulty of establishing clear boundaries between these lesions and true neoplasms. Malformations as well as granulomatous, reparative and inflammatory lesions are excluded. To facilitate histological identification of each entity, brief definitions and illustrations are appended.

The classification is based on the type of tissue of which the tumour is composed, whenever this can be determined. Accordingly, tumours and tumour-like lesions of the following tissues are distinguished: fibrous tissue, adipose tissue, muscle tissue, blood vessels, lymph vessels, synovial tissue, mesothelial tissue, peripheral nerves, sympathetic ganglia, paraganglionic structures, pluripotential mesenchyme, and embryonic structures. Three additional categories comprise tumours of possible extra-gonadal germ cell origin, tumours of disputed or uncertain histogenesis, and lesions of non-neoplastic or questionably neoplastic type of interest because of their resemblance to true neoplasms.

Most of these broad categories are subdivided into a benign and a malignant group. This subdivision is not meant to imply that malignant soft tissue tumours tend to originate from their benign counterparts. In fact, malignant transformation of soft tissue tumours is an exceedingly rare event, with the exception perhaps of the occasional transformation of neurofibromas into malignant Schwannomas.

Subtypes are given where they are believed to be of value in predicting the clinical behaviour. A combination of histogenetic and descriptive terms

(e.g., pleomorphic liposarcoma) is used to designate these tumours. Eponyms and synonyms are employed only if they have been widely used in the literature or if their use is considered to be important for an understanding of the disease; in such cases, the preferred term is given first, followed by the synonym in square brackets. In some instances, outdated or imprecise names have been changed if the premises for their original designation are no longer acceptable; thus, "granular cell myoblastoma" has been changed to "granular cell tumour" because the muscle origin of this tumour has been disputed by most investigators.

In addition to the tumours of known histogenesis, there are tumours of typical morphology that fail to give any clue as to their tissue type (categories XIV and XV). Classification of these tumours has been tentatively based upon some other characteristics, such as the size, the shape and the staining characteristics of the tumour cells and their arrangement and pattern (e.g., alveolar soft part sarcoma).

Finally, there are soft tissue tumours of unusual or bizarre morphology that will not fit readily into any of the suggested tumour categories and for the time being will have to be designated as "tumour type unclassified". Perhaps 10-15% of malignant soft tissue tumours and a smaller number of benign tumours fall into this category. Terms such as spindle-cell sarcoma or round-cell sarcoma should be avoided in classifying tumours of unknown type, because such terms are meaningless for the correlation of morphology with clinical behaviour.

Difficulties in typing soft tissue tumours

Classification of soft tissue tumours on a histogenetic basis is not always easily accomplished. It is simple with benign soft tissue tumours because the cytological characteristics and the specific products of the tumour cells closely resemble those of normal tissue. Thus, lipomas or leiomyomas composed of only slightly modified fat or smooth muscle cells usually pose no particular problem. Classification of malignant soft tissue tumours, however, is often difficult. The cells of malignant tumours frequently differ in appearance and function from those of the prototype tissue and sometimes are recognizable only by their superficial resemblance to some phases of normal embryonic tissue development.

Most soft tissue tumours consist of a tissue type that is normally present at their anatomic site of origin, but this is not invariably the case. Some soft tissue tumours, particularly malignant ones, produce tissue types apparently foreign to the part of the body from which they arise. Rhabdomyosarcomas, for example, occur in the bile duct region and the vagina, i.e., in areas where striated muscle tissue is normally not formed. Synovial sarcomas develop occasionally in the abdominal wall far removed from any normal synovial structure. Most likely these tumours arise from

persisting or newly formed foci of multipotential mesenchyme or from some incompletely differentiated kinds of tissue.

Caution in the interpretation of the tissue type must be exercised if the cells are associated with collagen production. Various types of tumour cells, such as synovioblasts, mesothelial cells, Schwann cells and histiocytes, are capable of producing collagen fibres and the mere association of cells and collagen does not necessarily indicate that the cells are fibroblasts. Likewise, the presence of lipid in tumour cells or tissue is a fairly common occurrence, yet the finding of this feature alone does not warrant the diagnosis of lipoma or liposarcoma. In fact, lipid in tumours is frequently the result of altered cellular metabolism associated with early tissue degeneration.

Diagnostic procedures

Accurate diagnosis requires adequate material representative of the main characteristics of the tumour. Such material can be obtained by incisional or excisional biopsy, and occasionally by needle biopsy. In most instances, particularly if major surgery depends upon an accurate diagnosis, examination by open surgical biopsy is to be preferred. Biopsy should be sufficiently deep, and should include viable tumour tissue as well as portions of the surrounding tumour bed. Incisional biopsy has been condemned by some because of the supposed but unproven danger of promoting the spread of malignant cells; if surgical trauma is kept to a minimum, the merits of open incisional biopsy certainly outweigh its risks.

Frozen-section diagnosis is useful in those rare cases in which immediate therapeutic action is required. This method as applied to soft tissue tumours requires judgement and experience in order to avoid serious errors and, in our opinion, should be used only by specially qualified pathologists. Likewise, needle or aspiration biopsy of soft tissue may be useful in the hands of a competent pathologist but it seems doubtful whether it can effectively replace open biopsy as a routine procedure. Obviously those tumours that are already difficult to diagnose with adequate material are more liable to be misinterpreted if only a minute and possibly non-representative portion of the lesion can be examined. Exfoliative cytology has its special and established place in the diagnosis of mesotheliomas.

Paraffin sections of adequately fixed material stained with haematoxylin and eosin will usually suffice for diagnosis, but selective staining procedures may be necessary in the evaluation of occasional problem cases. In studying soft tissue tumours, such staining procedures are used for myofibrils, lipid, glycogen, melanin, mucin, acid and sulfated mucopolysaccharides, reticulum, elastic fibres, iron, and others. At times,

treatment of the sections prior to staining with diastase or hyaluronidase assists in arriving at a diagnosis. The former procedure, combined with the periodic acid Schiff (PAS) reaction, helps to separate glycogen from other PAS-positive material; treatment with hyaluronidase combined with various mucin stains allows distinction of the acid mucopolysaccharides produced by liposarcomas (and other soft tissue tumours) from the sulfated mucopolysaccharides elaborated by chondroid neoplasms. Other histochemical and enzymatic techniques, many still in their experimental stage, may also be useful in the localization of specific structural elements.

Methods that may be helpful in the study of soft tissue tumours also include phase contrast and electron microscopy, small-angle X-ray diffraction, fluorescent antibody techniques, and microangiography. Tissue culture *in vitro* often allows recognition of the prototype cells, even if the parent tumour is poorly differentiated. This method is of practical value in differential diagnosis of neuroblastoma and Ewing's sarcoma. Chemical analysis of tumour tissue or of isolated cellular elements may also yield information regarding the products of the tumour cells or their function and so may lead to a more precise histogenetic classification.

In addition to histological study, detailed inspection of the gross specimen and information as to the operative findings, particularly the relationship of the tumour to skin, fascia, tendon sheath, bone or joint, are essential to diagnosis. Sometimes, however, too much reliance upon the gross inspection may be misleading; such features as encapsulation, poor circumscription, and infiltration may be deceptive as to the true growth potential of the tumour and may invite inadequate or excessive therapy. Shelling out or enucleation of apparently well circumscribed or encapsulated malignant soft tissue tumours should be discouraged. Such procedures are bound to lead to recurrence and complications, since often satellite nodules or groups of viable tumour cells are situated about the main tumour mass or in the capsular tissue.

Evidence of infiltrative growth may also be an unreliable guide to the clinical behaviour. Nodular fasciitis, proliferative myositis and other innocuous lesions insidiously infiltrate neighbouring tissues in a sarcoma-like manner and yet these lesions are perfectly benign and are treated effectively by simple excision. In most cases, therefore, it is best to plan definitive therapy only after the diagnosis has been established by open biopsy. The delay in treatment caused by the biopsy procedure is insignificant compared with the therapeutic hazards of an erroneous diagnosis.

Correlation between histological and other findings

Accurate classification of soft tissue tumours requires close correlation between clinical features and histology. The information provided by the clinical history, physical examination, radiography and laboratory studies

is important and sometimes indispensable for a correct diagnosis. Knowledge of the age and the sex of the patient and the localization of the tumour may be significant. For reasons that are still poorly understood, virtually every well-defined soft tissue tumour has a predilection for certain age periods and anatomic sites; moreover, some soft tissue tumours occur more frequently in men, others in women. These interrelationships between tumour type and certain clinical features are well illustrated by the predominance of embryonal rhabdomyosarcoma in children, the predilection of juvenile aponeurotic fibroma for the palmar region of the hand, and the almost exclusive occurrence of juvenile angiofibroma in male patients. The clinical behaviour of some tumours varies according to the anatomic site. Thus, fibromatosis is more likely to recur and behave in an aggressive manner when it is situated in the muscles of the shoulder or neck region than when located at other sites.

Environmental and genetic factors, revealed by careful history-taking, may also contribute to the understanding of the disease. The specific role of these factors is evident from the occurrence of mesothelioma following exposure to asbestos dust, the occasional development of sarcomas secondary to radiotherapy or prolonged lymph stasis, the familial incidence of neurofibromatosis, and the association of mesenteric fibromatosis and familial intestinal polyposis in Gardner's syndrome.

Vital information may be obtained from certain laboratory studies. Thus, the demonstration of catecholamine derivatives in the urine may suggest the presence of pheochromocytoma or, as more recently shown, the presence of neuroblastoma, ganglioneuroblastoma, or ganglioneuroma.

Obviously, the fact that histology is to date the most reliable guide for making an accurate diagnosis and for predicting the clinical behaviour does not preclude the need for clinical information. Only integration of all morphological and clinical data, achieved by close co-operation between clinician and pathologist, assures the ultimate goal of reaching a correct diagnosis and providing adequate therapy for the patient.

HISTOLOGICAL TYPING OF SOFT TISSUE TUMOURS

I. TUMOURS AND TUMOUR-LIKE LESIONS OF FIBROUS TISSUE

A. FIBROMAS

1. Fibroma durum
2. Fibroma molle [fibrolipoma]
3. Dermatofibroma [histiocytoma, sclerosing haemangioma]
4. Elastofibroma (dorsi)

B. FIBROMATOSIS

1. Cicatricial fibromatosis
2. Keloid
3. Nodular fasciitis [pseudosarcomatous fibromatosis]
4. Irradiation fibromatosis
5. Penile fibromatosis [Peyronie's disease]
6. Fibromatosis colli
7. Palmar fibromatosis
8. Juvenile aponeurotic fibroma [calcifying fibroma]
9. Plantar fibromatosis
10. Nasopharyngeal fibroma [juvenile angiofibroma]
11. Abdominal fibromatosis [abdominal desmoid]
12. Fibromatosis or aggressive fibromatosis [extra-abdominal desmoid]
13. Congenital generalized fibromatosis

C. DERMATOFIBROSARCOMA PROTUBERANS

D. FIBROSARCOMA

II. TUMOURS AND TUMOUR-LIKE LESIONS OF ADIPOSE TISSUE

A. BENIGN

1. Lipoma (including fibrolipoma, angiolipoma, etc)
2. Intramuscular lipoma [infiltrating lipoma]

3. Hibernoma
4. Angiomyolipoma (of renal origin)
5. Myelolipoma
6. Lipoblastomatosis [foetal lipoma]
7. Diffuse lipomatosis

B. MALIGNANT

1. Liposarcoma
 - a. predominantly well-differentiated
 - b. predominantly myxoid [embryonal]
 - c. predominantly round-cell
 - d. predominantly pleomorphic (poorly differentiated)
 - e. mixed type (combining features of a, b, c, or d)

III. TUMOURS OF MUSCLE TISSUE

A. SMOOTH MUSCLE

1. Benign
 - a. Leiomyoma
 - b. Angiomyoma [vascular leiomyoma]
 - c. Epithelioid leiomyoma [bizarre leiomyoma, leiomyoblastoma]
2. Malignant
 - a. Leiomyosarcoma

B. STRIATED MUSCLE

1. Benign
 - a. Rhabdomyoma
2. Malignant
 - a. Rhabdomyosarcoma
 - (1) predominantly embryonal
 - (2) predominantly alveolar
 - (3) predominantly pleomorphic
 - (4) mixed (combining the features of (1), (2), or (3))

IV. TUMOURS AND TUMOUR-LIKE LESIONS OF BLOOD VESSELS

A. BENIGN

1. Haemangioma
 - a. Benign haemangioendothelioma
 - b. Capillary haemangioma [juvenile haemangioma]
 - c. Cavernous haemangioma
 - d. Venous haemangioma
 - e. Racemose [cirroid] haemangioma (arterial, venous, arteriovenous)
2. Intramuscular haemangioma (capillary, cavernous or arteriovenous)
3. Systemic haemangiomatosis
4. Haemangiomatosis with or without congenital arteriovenous fistula
5. Benign haemangiopericytoma
6. Glomus tumour [glomangioma]
7. Angiomyoma [vascular leiomyoma]
8. "Haemangioma" of granulation-tissue type [granuloma pyogenicum]

B. MALIGNANT

1. Malignant haemangioendothelioma [angiosarcoma]
2. Malignant haemangiopericytoma

V. TUMOURS AND TUMOUR-LIKE LESIONS OF LYMPH VESSELS

A. BENIGN

1. Lymphangioma
 - a. capillary
 - b. cavernous
 - c. cystic [hygroma]
2. Lymphangiomyoma
3. Systemic lymphangiomatosis

B. MALIGNANT

1. Malignant lymphangioendothelioma [lymphangiosarcoma]

VI. TUMOURS OF SYNOVIAL TISSUES

A. MALIGNANT

1. Synovial sarcoma [malignant synovioma]
 - a. predominantly biphasic (spindle-cell *and* epithelioid patterns)
 - b. predominantly monophasic (spindle-cell *or* epithelioid pattern)

B. BENIGN

1. Benign synovioma

VII. TUMOURS OF MESOTHELIAL TISSUE

A. BENIGN MESOTHELIOMA

1. predominantly epithelioid
2. predominantly fibrous (spindle-cell)
3. biphasic

B. MALIGNANT MESOTHELIOMA

1. predominantly epithelioid
2. predominantly fibrous (spindle-cell)
3. biphasic

VIII. TUMOURS AND TUMOUR-LIKE LESIONS OF PERIPHERAL NERVES

A. BENIGN

1. Traumatic neuroma [amputation neuroma]
2. Neurofibroma
3. Neurilemoma [Schwannoma]
4. Neurofibromatosis [von Recklinghausen's disease]

B. MALIGNANT

1. Malignant Schwannoma [neurogenic sarcoma, neurofibrosarcoma]
2. Peripheral tumours of primitive neuroectoderm

IX. TUMOURS OF SYMPATHETIC GANGLIA

A. BENIGN

1. Ganglioneuroma

B. MALIGNANT

1. Neuroblastoma [sympathicoblastoma, symphathicogonioma]
2. Ganglioneuroblastoma

X. TUMOURS OF PARAGANGLIONIC STRUCTURES

A. PHAEOCHROMOCYTOMA

1. Benign
2. Malignant

B. CHEMODECTOMA [non-chromaffin paraganglioma]

1. Benign
2. Malignant

C. PARAGANGLIOMA, UNCLASSIFIED

XI. TUMOURS AND TUMOUR-LIKE LESIONS OF PLURIPOTENTIAL MESENCHYME

A. BENIGN

1. Mesenchymoma

B. MALIGNANT

1. Malignant mesenchymoma

XII. TUMOURS OF VESTIGIAL EMBRYONIC STRUCTURES

A. BENIGN

1. Chordoma

B. MALIGNANT

1. Malignant chordoma

XIII. TUMOURS OF POSSIBLE EXTRAGONADAL GERM-CELL ORIGIN

A. BENIGN

1. Teratoma [dermoid cyst]

B. MALIGNANT

1. Teratocarcinoma
2. Embryonal carcinoma
3. Choriocarcinoma

XIV. TUMOURS OF DISPUTED OR UNCERTAIN HISTOGENESIS

A. BENIGN

1. Granular cell tumour [granular cell "myoblastoma"]
2. Chondroma of soft parts
3. Osteoma of soft parts
4. Nasal glioma [ganglioglioma]
5. Pacinian tumour
6. Adenomatoid tumour of genital tract
7. Myxoma
8. Melanotic progonoma [retinal anlage tumour, melanotic neuroectodermal tumour of infancy]
9. Fibrous hamartoma of infancy

B. MALIGNANT

1. Alveolar soft-part sarcoma [malignant organoid granular cell "myoblastoma"]

2. Malignant granular cell tumour [malignant (nonorganoid) granular cell "myoblastoma"]
3. Chondrosarcoma of soft parts
4. Osteosarcoma of soft parts
5. Malignant giant-cell tumour of soft parts
6. Malignant fibroxanthoma [malignant histiocytoma]
7. Kaposi's sarcoma
8. Clear-cell sarcoma of tendons and aponeuroses

XV. NON-NEOPLASTIC OR QUESTIONABLY NEOPLASTIC LESIONS OF SOFT TISSUES, OF INTEREST BECAUSE OF THEIR RESEMBLANCE TO TRUE NEOPLASMS

A. XANTHOMA GROUP

1. Fibroxanthoma [fibrous histiocytoma]
 - a. Atypical fibroxanthoma
2. Xanthoma
3. Juvenile xanthogranuloma [naevoxanthoendothelioma]
4. Retroperitoneal xanthogranuloma (Oberling)
5. Nodular tenosynovitis [giant-cell tumour of tendon sheath] and pigmented villonodular synovitis

B. GANGLION

C. LOCALIZED MYXOEDEMA

D. MYOSITIS OSSIFICANS

E. PROLIFERATIVE MYOSITIS

XVI. SOFT-TISSUE TUMOUR, UNCLASSIFIED

EXPLANATORY NOTES

I. TUMOURS AND TUMOUR-LIKE LESIONS OF FIBROUS TISSUE

A. FIBROMAS

1. *Fibroma durum*. A benign and frequently pedunculated, well circumscribed dense growth of fully matured and richly collagenous fibrous connective tissue occurring on the body surface and mucous membranes. Many so-called "fibromas" are examples of hyperplastic fibrous tissue rather than true neoplasms.

2. *Fibroma molle [fibroliipoma]*. A benign and usually pedunculated growth made up of a mixture of mature fibrous connective tissue and adult-type fat occurring on the body surface.

3. *Dermatofibroma [histiocytoma, sclerosing haemangioma]*. A benign, non-encapsulated, superficial lesion, characterized by an intimate mixture of histiocyte and fibroblast-like cells associated with varying amounts of collagen and thin-walled blood vessels. Frequently, lipid macrophages and siderophages are prominent features of the lesion.

4. *Elastofibroma (dorsi)*. A slow-growing, benign, poorly circumscribed fibrous growth, which is characterized by the association of collagen bundles and homogeneous acidophilic fibrillary or globular material staining similarly to elastic tissue. The lesion is deep-seated and affects almost exclusively the subscapular region of elderly individuals. Bilateral involvement has been observed.

B. FIBROMATOSIS

1. *Cicatricial fibromatosis*. A non-metastasizing progressive overgrowth of fibrous tissue arising in association with a scar.

2. *Keloid*. A superficial nodular, parvicellular, fibrous growth, characterized by well-defined interlacing broad bands of homogeneous, acidophilic collagen. The lesion usually follows some form of injury to the skin

and is found mainly in Negroes. Unlike hypertrophic scars, which do not show the characteristic thick, glassy collagen bundles, the lesion tends to recur.

3. *Nodular fasciitis [pseudosarcomatous fibromatosis]*. A benign and probably reactive fibroblastic growth extending as a solitary nodule from the superficial fascia into the subcutaneous fat or, less frequently, into the subjacent muscle. Confusion with a sarcoma is possible because of its cellularity, its mitotic activity, its richly mucoid stroma, and its rapid growth. Other fibroblastic proliferations, such as proliferative myositis (XV/E), are probably akin to this lesion. Nodular fasciitis is most common in the upper extremity, the trunk and the neck region of young adults.

4. *Irradiation fibromatosis*. A benign, infiltrating and often aggressive growth of richly collagenous fibrous connective tissue consequent to tissue injury by radiation. The frequent presence of bizarre cells should not be mistaken for evidence of malignancy. Differentiation from the rare post-irradiation fibrosarcoma might be difficult.

5. *Penile fibromatosis [Peyronie's disease]*. A dense, infiltrating, fibrous growth affecting the fascial structures and the fibrous septa of the corpora cavernosa and the corpus spongiosum of the penis. The condition occurs chiefly in adults between 40 and 65 years of age and is occasionally associated with palmar and plantar fibromatoses. Secondary ossification has been observed occasionally.

6. *Fibromatosis colli*. A benign, poorly circumscribed fibrous growth of unknown histogenesis arising in the sternocleidomastoid muscle of infants and small children. Contraction of the fibrous tissue may lead to wry-neck or torticollis. Bilateral forms have been observed.

7. *Palmar fibromatosis*. A benign, nodular, infiltrating, fibrous lesion of variable cellularity originating in the palmar aponeuroses and leading to contracture of the fingers [Dupuytren's contracture]. Multiple lesions involving the feet as well as the hands are observed occasionally (see I/B/9, plantar fibromatosis).

8. *Juvenile aponeurotic fibroma [calcifying fibroma]*. A rare infiltrating fibrous growth affecting chiefly the muscles and the subcutaneous fat of the volar aspects of the hands. The growths apparently occur exclusively in children, adolescents and, rarely, young adults. Characteristically, the infiltrating collagenous tumour is associated with irregular foci of calcification and chondroid metaplasia. Local recurrence is frequent.

9. *Plantar fibromatosis*. A benign, nodular, infiltrating fibrous lesion of variable cellularity originating in the plantar aponeuroses and leading to contracture of the toes. This lesion is found mainly in adults. Multiple lesions involving the hands as well as the feet are observed occasionally (see I/B/7, palmar fibromatosis).

10. *Nasopharyngeal fibroma [juvenile angiofibroma]*. A locally invasive growth of more or less mature fibrovascular tissue arising in the wall of the nasopharynx and its vicinity and affecting almost exclusively male patients between 10 and 25 years of age. Spontaneous regression has been observed.

11. *Abdominal fibromatosis [abdominal desmoid]*. A locally aggressive infiltrating tumour-like fibroblastic growth of unknown pathogenesis arising from the musculo-aponeurotic structures of the rectus muscle and the adjacent muscles of the abdominal wall. It differs from a fibrosarcoma mainly in its uniform growth pattern, the abundance of collagen, and the paucity of mitotic figures. The lesion occurs most commonly in women during or following pregnancy but has also been observed in men and in small children of both sexes.

12. *Fibromatosis or aggressive fibromatosis [extra-abdominal desmoid]*. A non-metastasizing tumour-like fibroblastic growth of unknown pathogenesis involving voluntary muscle as well as aponeurotic and fascial structures. Histologically, it is indistinguishable from an abdominal fibromatosis (I/B/11). The lesion has a strong tendency to local recurrence and aggressive, infiltrating growth. It is most common in the shoulder girdle, the thigh, and the buttock of young adults.¹

13. *Congenital generalized fibromatosis*. An extremely rare mesenchymal and predominantly fibroblastic growth developing simultaneously at multiple sites prior to birth or during the first year of life. Fatal cases with widespread visceral involvement have been observed. Familial incidence has been recorded.

C. DERMATOFIBROSARCOMA PROTUBERANS

A cellular tumour of disputed histiocytic or fibroblastic origin composed of small, uniform cells arranged in a cartwheel pattern. It usually forms a protruding nodular or multinodular mass by infiltration of the entire dermis and the subcutaneous fat. The tumour has a tendency to recur locally after simple excision. Cases with metastases have been recorded.

¹ The association of fibromatosis, familial intestinal polyposis, osteomas and cutaneous epithelial cysts is known as Gardner's syndrome.

D. FIBROSARCOMA

A malignant circumscribed or infiltrating tumour composed of reticulin and collagen, which produces predominantly spindle-shaped cells showing no evidence of other forms of cellular differentiation. The histological picture consists chiefly of interlacing, densely cellular fascicles of more or less uniform spindle cells, often forming a herring-bone pattern. A characteristic feature is the close relationship between cells and reticulin fibres. Mitotic figures are a constant feature of fibrosarcoma. It is possible that some ill-defined pleomorphic sarcomas are of fibroblastic origin. The tumour is capable of metastasis, chiefly via the blood stream.

II. TUMOURS AND TUMOUR-LIKE LESIONS OF ADIPOSE TISSUE

A. BENIGN

1. *Lipoma (including fibrolipoma, angiolipoma, etc.)*. A benign growth made up exclusively of mature adipose tissue cells showing no evidence of cellular atypia. Lipomas arising in the panniculus adiposus are usually encapsulated; those arising elsewhere are frequently unencapsulated and less well demarcated. Lipomas undergoing myxoid changes should not be confused with a well-differentiated myxoid liposarcoma.

2. *Intramuscular lipoma [infiltrating lipoma]*. A benign proliferation of mature adipose tissue infiltrating striated muscle. The absence of cellular atypia serves to distinguish the lesion from a well-differentiated liposarcoma.

3. *Hibernoma*. A benign, lobulated, and encapsulated tumour made up of granular or vacuolated, round, acidophilic cells having the appearance of brown fat. Hibernoma usually involves the shoulder or neck region of young adults.

4. *Angiomyolipoma (of renal origin)*. A benign neoplasm of hamartomatous nature consisting of a mixture of adipose tissue, thick-walled vascular structures, and smooth-muscle elements. The neoplasm is generally unencapsulated. This term is used here exclusively for tumours arising from the renal cortex. Angiomyolipoma is sometimes a feature of the tuberous sclerosis complex.

5. *Myelolipoma*. A rare, benign, unilateral or bilateral lesion made up of an intimate mixture of haematopoietic tissue and mature fat. It occurs in the adrenal gland or, less frequently, in the soft tissue of the retroperi-

toneum and the pelvis. Unlike extramedullary haematopoiesis, the lesion is unassociated with haematopoietic disorders.

6. *Lipoblastomatosis* [foetal lipoma]. A benign, lobulated, lipoblastic growth resembling typical foetal fat. The lesion, which is easily confused with a myxoid liposarcoma, predominates in children during the first year of life and presents either as a localized, lipoma-like growth or as a diffuse infiltrating process. Maturation towards a typical lipoma has been observed in consecutive biopsies.

7. *Diffuse lipomatosis*. A diffuse, infiltrating proliferation of mature adipose tissue showing no evidence of cellular atypia. Large examples of this lesion may involve sizable portions of an extremity or the trunk. It chiefly affects children and is exceedingly rare during adult life.

B. MALIGNANT

1. *Liposarcoma*. A malignant infiltrating neoplasm, characterized by the presence of atypical lipoblasts in varying stages of differentiation. The histological picture of liposarcoma varies from well-differentiated to cellular or extremely pleomorphic types. Whenever possible liposarcoma should be subtyped according to the predominant cell pattern (II/B/1/a, b, c, d and e). The biological behaviour varies with the degree of differentiation. Metastases are more frequent among the less differentiated (round-cell and pleomorphic) types.

III. TUMOURS OF MUSCLE TISSUE

A. SMOOTH MUSCLE

1. Benign

a. *Leiomyoma*. A benign and occasionally richly vascular tumour of smooth muscle cells showing little variation in their appearance and characterized by the presence of non-striated myofibrils within their cytoplasm. Collagen formation, present in all leiomyomas, may be excessive and at times may obscure the basic structure of the tumour. The tumour occurs in superficial and deep locations.

b. *Angiomyoma* [vascular leiomyoma]. A benign, well-circumscribed and frequently tender or painful tumour, consisting of convoluted thick-walled vessels associated with bundles of well-differentiated smooth-muscle elements. The tumour occurs most commonly in the wrist and ankle region.

c. *Epithelioid leiomyoma* [bizarre leiomyoma, leiomyoblastoma]. A peculiar smooth-muscle tumour, characterized by predominantly rounded or polygonal cells with acidophilic cytoplasm and a clear space partially or completely surrounding the nucleus. Mitotic figures are scanty or absent in most cases. Transitions towards typical elongated smooth-muscle cells are seen occasionally. The tumour, which sometimes reaches an enormous size, usually arises from the muscle coat of the stomach wall of adult patients. Less commonly it occurs in the mesentery, the omentum, or other areas. The behaviour is very difficult to predict. The great majority of epithelioid leiomyomas follow a benign clinical course; a few, however, are known to have metastasized.

2. Malignant

a. *Leiomyosarcoma*. A malignant, occasionally richly vascular neoplasm of elongated, acidophilic cells containing a varying number of non-striated myofibrils and showing frequently a perinuclear clear space. The cells tend to be arranged in sharply intersecting bundles and fascicles. Helpful criteria for differential diagnosis from leiomyoma are the greater degree of cellularity, the presence of cellular pleomorphism, including tumour giant cells, and, most important, the presence of typical and atypical mitotic figures. Occasionally the parallel arrangement of the reticulin fibres may be helpful in distinguishing the tumour from fibrosarcoma. Leiomyosarcomas may occur at any site, including the wall of large vessels.

B. STRIATED MUSCLE

1. Benign

a. *Rhabdomyoma*. A benign tumour generally consisting of polygonal, frequently vacuolated (glycogen-containing) cells having a finely granular deeply acidophilic cytoplasm. Cells with cross-striations are fairly common. The tumour is rare and the majority of cases have been observed in the upper neck region, the tongue, the pharyngeal wall, and the vicinity of the larynx.

2. Malignant

a. *Rhabdomyosarcoma*. A highly malignant tumour of rhabdomyoblasts in varying stages of differentiation with or without intracellular myofibrils, and with or without cross-striations. Cytology and growth pattern vary greatly and three types can be distinguished: predominantly embryonal (including the botryoid type), alveolar and pleomorphic

(III/B/2/a, 1, 2 and 3). The two former types prevail in children and adolescents. Mixed forms may occur. The embryonal and alveolar types of the tumour may arise in sites where skeletal muscle is not normally present. Special staining techniques may be necessary for the demonstration of cross-striations. Lymphatic and blood-borne metastases are common.

IV. TUMOURS AND TUMOUR-LIKE LESIONS OF BLOOD VESSELS

A. BENIGN

1. *Haemangioma*. A benign non-circumscribed lesion consisting of proliferated blood vessels of various types. In the lesions belonging to this group, distinction between tissue malformations (hamartomas) and true tumours is especially difficult.

a. *Benign haemangioendothelioma*. A benign and largely solid mass of endothelial cells of typical appearance identifiable by the formation of capillaries or other vascular structures in some places. Frequently, this lesion is not clearly separable from capillary haemangioma. The growth is most common in the head and neck area of small children. Reticulin stains often help in the recognition of these lesions.

b. *Capillary haemangioma [juvenile haemangioma]*. A benign lesion composed predominantly of small vascular channels, mostly of capillary size, lined by a single layer of endothelial cells.

c. *Cavernous haemangioma*. A benign lesion composed predominantly of cavernous vascular structures lined by a single layer of endothelial cells.

d. *Venous haemangioma*. A benign lesion composed of irregular lumina to large-sized vessels, predominantly of the venous type. Isolated smooth muscle elements, fibrous tissue, and fat may be associated with the lesion.

e. *Racemose [cirsoid] haemangioma (arterial, venous, arteriovenous)*. A lesion resembling a malformation composed of tortuous, thick-walled blood vessels of the venous and arterial type. Those that are predominantly arterial are generally found in the region of the head.

f. *Intramuscular haemangioma (capillary, cavernous or arteriovenous)*. A benign, non-systemic, poorly circumscribed vascular growth slowly infiltrating striated muscle. Either capillary or cavernous structures may predominate. The lesion is found chiefly in young adults. It should not be confused with malignant vascular tumours.

3. *Systemic haemangiomatosis*. A condition involving one or more organs or tissues and characterized by multicentric or diffuse haemangiomatic lesions. Rendu-Osler-Weber disease, Sturge-Weber disease, the Mafucci syndrome, the Bourneville syndrome, and Hippel-Lindau disease are forms of systemic hemangiomatosis.

4. *Haemangiomatosis with or without congenital arteriovenous fistula*. Regional or diffuse proliferation of capillaries or thin-walled vascular structures with or without a congenital arteriovenous fistula. Sometimes this lesion is accompanied by overgrowth of fat and/or bone.

5. *Benign haemangiopericytoma*. A tumour characterized by the proliferation of round, oval or spindle-shaped cells of rather uniform size, surrounded by reticulin fibrils and arranged about vascular spaces lined by a single layer of endothelial cells. The tumour is uncommon, and a clear separation from other well-vascularized mesenchymal tumours is often difficult and may cause a considerable problem in the differential diagnosis. It is not always easy to predict the clinical course on the basis of the histological findings.

6. *Glomus tumour [glomangioma]*. A benign tumour made up of acidophilic, epithelioid, round cells of uniform size with large oval nuclei, probably derived from the neuromyoarterial glomus. The cells are usually intimately associated with vascular structures of varying size and often blend with smooth muscle tissue. The tumour may occur anywhere, but is most common in the distal portions of the extremities.

7. *Angiomyoma [vascular leiomyoma]*. A benign, well-circumscribed and frequently tender or painful tumour consisting of convoluted thick-walled vessels associated with bundles of well-differentiated smooth-muscle elements. The tumour occurs most commonly in the wrist and ankle region and is frequently tender or painful.

8. "*Haemangioma*" of granulation-tissue type [*granuloma pyogenicum*]. A benign, solitary, raised lesion of the skin and mucous membranes having the microscopic appearance of a lobulated capillary haemangioma or richly vascular granulation tissue. Secondary features, such as surface ulceration, chronic inflammation, and fibrosis are common. The initial rapid growth and the tendency of the lesion to occur during adult life help to distinguish it from capillary haemangioma.

B. MALIGNANT

1. *Malignant haemangioendothelioma [angiosarcoma]*. A highly malignant neoplasm characterized by the formation of irregular anastomosing

vascular channels lined by one or more layers of atypical endothelial cells, often of immature appearance. The female breast is one of the commonest sites of the tumour. Metastases are usually blood-borne.

2. *Malignant haemangioepithelioma*. A malignant tumour characterized by the proliferation of rather uniform, round, oval or spindle-shaped cells about vascular spaces of varying size lined by a single layer of endothelial cells. Clear separation from other well-vascularized mesenchymal tumours, such as synovial sarcoma, mesothelioma, and malignant fibroxanthoma, is often exceedingly difficult and may cause a problem in the differential diagnosis.

V. TUMOURS AND TUMOUR-LIKE LESIONS OF LYMPH VESSELS

A. BENIGN

1. *Lymphangioma*. A benign growth composed exclusively of lymph vessels of various size lined by a single layer of endothelial cells. The lesion is often congenital and is probably the result of a tissue malformation during the early development of the lymphatic system. Lymphangiomas should be typed as capillary, cavernous, or cystic (V/A/1/a, b and c). The cavernous and cystic forms [hygroma] of this tumour are most frequent in the cervical, mediastinal, and retroperitoneal regions of infants and children. Capillary lymphangiomas are exceedingly rare and are difficult to distinguish from capillary haemangiomas.

2. *Lymphangiomyoma*. A growth composed of bundles of smooth-muscle tissue about cavernous or slit-like, endothelial-lined lymph spaces. Aggregates of lymphocytes may or may not be found in association with the smooth-muscle tissue. The tumour has been observed only in the mediastinum and retroperitoneum in close association with the thoracic duct and its tributaries. Chylothorax and pulmonary complications are common.

3. *Systemic lymphangiomatosis*. A condition in which one portion of the body is altered by excessive growth of lymphangiomatous structures often causing deformities. Children are almost exclusively affected.

B. MALIGNANT

1. *Malignant lymphangi endothelioma [lymphangiosarcoma]*. A malignant neoplasm marked by the formation of irregular lymphatic struc-

tures lined by one or more layers of endothelial cells showing a varying degree of cellular atypia. So far this tumour has been observed exclusively in conjunction with chronic lymph stasis, usually secondary to radical mastectomy.

VI. TUMOURS OF SYNOVIAL TISSUES

A. MALIGNANT

1. *Synovial sarcoma [malignant synovioma]*. A malignant neoplasm showing a biphasic cellular pattern composed of clefts or acinar structures lined by epithelial-like cells, with or without formation of mucoid material, and separated by reticulin- and collagen-forming fibrosarcoma-like spindle-cell areas of varying cellular density. Calcification and hyalinization are frequent features. There is also a monophasic form in which the gland-like spaces are exceedingly rare and can be found only after careful examination of multiple sections; this often makes it very difficult to distinguish the tumour from a fibrosarcoma. Synovial sarcoma is capable of metastasizing through the blood stream and less frequently through the lymphatics. Most synovial sarcomas occur in young adults and usually arise from tissues in the vicinity of large joints (for subtypes see VI/A/1/a and b).

B. BENIGN

1. *Benign synovioma*. Whether true benign tumours of synovial tissues exist is controversial. Nodular tenosynovitis and pigmented villonodular synovitis are discussed on page 43 (XV/A/5).

VII. TUMOURS OF MESOTHELIAL TISSUE (MESOTHELIOMAS)

Tumours arising from the mesothelial lining of the coelomic cavities and consisting of a variable mixture of epithelioid and spindle-cell elements. Whenever possible, the predominant cell characteristics should be specified (for subtypes see VII/A/1, 2 and 3; VIII/B/1, 2 and 3). Characteristically, the tumours form a tubular, papillary, or tubulo-papillary growth pattern, but occasionally they are difficult to distinguish from fibromas or fibrosarcomas. Diffuse and localized forms occur. Patients with mesothelioma frequently give a history of exposure to asbestos dust.

VIII. TUMOURS AND TUMOUR-LIKE LESIONS OF PERIPHERAL NERVES

A. BENIGN

1. *Traumatic neuroma [amputation neuroma]*. A benign non-neoplastic overgrowth of nerve fibres, Schwann cells, and scar tissue occurring at the proximal end of a severed nerve trunk.

2. *Neurofibroma*. A benign localized or diffuse tumour consisting of a mixture of Schwann cells and fibroblasts accompanied by loosely arranged collagen fibres and mucinous material. Plexiform neurofibromas are the result of growth within and about a preformed nerve, giving the nerve trunk a tortuous, thickened, and plexiform appearance. Neurites can be frequently demonstrated within these tumours. Malignant transformation of neurofibromas occurs.

3. *Neurilemoma [Schwannoma]*. A benign and usually well demarcated or encapsulated tumour, most probably of nerve-sheath origin. Characteristically, an Antoni type A pattern, with regimentation of the nuclei in twisted rows or palisades (Verocay bodies), and an Antoni type B pattern, with loosely arranged cells within a wide-meshed, microcystic fibrillar stroma, can be distinguished. Perivascular hyalinization is common. Secondary features, such as haemorrhage, thrombosis, phagocytosis of lipid and haemosiderin, and cystic changes are frequent findings, usually occurring in tumours that have been present for many months or years.

4. *Neurofibromatosis [von Recklinghausen's disease]*. A hereditary systemic disease characterized chiefly by the presence of one or more neurofibromas and multiple café-au-lait spots. Associated lesions include skeletal deformities and elephantiasis.

B. MALIGNANT

1. *Malignant Schwannoma [neurogenic sarcoma, neurofibrosarcoma]*. A malignant and usually densely cellular tumour consisting of rather plump spindle-shaped or ovoid cells of Schwannian origin, generally showing little cellular pleomorphism and often accompanied by collagen fibres. Nuclear palisading, as well as an arrangement of the cells in groups, nests, cords, or whorls are features helpful in differential diagnosis. Origin in a pre-existing neurofibroma is frequent, but origin in a neurilemoma, if it ever occurs, must be exceedingly rare. For this reason the term malignant neurilemoma should be avoided. Distant metastases are frequent in the highly cellular form of this tumour.

2. *Peripheral tumours of primitive neuroectoderm*. These are a closely related group of tumours occurring outside the central nervous system and simulating neural crest tissue in various stages of development. Some are indistinguishable from their central nervous system counterpart. They include neuroepitheliomas, medulloepitheliomas, medulloblastomas, ependymomas, and olfactory neuroepitheliomas [olfactory neuroblastomas]. Neuroepitheliomas, medulloepitheliomas, medulloblastomas and ependymomas are malignant tumours capable of metastasis, but metastasis of olfactory neuroepithelioma is very rare.

IX. TUMOURS OF SYMPATHETIC GANGLIA

A. BENIGN

1. *Ganglioneuroma*. A benign tumour composed of mature ganglion cells (with or without Nissl granules and satellite cells) associated with well-differentiated neurofibromatous elements.

B. MALIGNANT

1. *Neuroblastoma [sympathicoblastoma, sympathicogonioma]*. A highly malignant tumour of undifferentiated neuroblasts (sympathicoblasts). The neuroblasts are usually of small size with darkly staining nuclei and indistinct cytoplasm. Arrangement of the cells in spheroid groups about a central tangle of fibrillary material (Homer-Wright rosettes) is a characteristic feature. The tumour occurs predominantly in children under the age of 4 years, usually in close association with the adrenal medulla or the sympathetic chain.

2. *Ganglioneuroblastoma*. A tumour of varying degrees of malignancy made up of a mixture of neuroblasts (sympathicoblasts) and ganglion cells in various stages of differentiation. Some of the tumours show a fairly uniform distribution of the tumour cells; others display a composite picture with alternating differentiated and undifferentiated areas. As in neuroblastoma, the majority of these tumours occur along the thoracolumbar sympathetic chain or in the adrenal gland. Ganglioneuroblastomas are most common in children under 5 years of age. Rarely regression of the tumour or maturation into a ganglioneuroma occurs.

Increased catecholamine levels and diarrhoea have been observed in patients with ganglioneuroma, ganglioneuroblastoma, and neuroblastoma.

X. TUMOURS OF PARAGANGLIONIC STRUCTURES

A. PHAEOCHROMOCYTOMA. A benign or malignant neoplasm of chromaffin cells arising from the adrenal medulla, aberrant adrenal medullary tissue, or from the organ of Zuckerkandl or similar paraganglia. It is characterized by its distinctive organoid growth pattern, the presence of intracellular chromaffin granules,¹ and the secretion of catecholamines. Paroxysmal or persistent hypertension and other vasomotor disorders are often associated with the tumour. It is difficult to predict the behaviour of this tumour from its morphology.

B. CHEMODUXTOMA [NON-CHROMAFFIN PARAGANGLIOMA]. A generally benign tumour of non-chromaffin, chemodectal tissue (carotid body, glomus jugulare, aortic body, intravagal body, etc.) showing an organoid growth pattern with nests of cells separated by vascular structures and connective tissue. These tumours can be multicentric. Malignant behaviour is exceedingly rare. As in most tumours of endocrine type, the presence of free tumour cells in blood vessels is not by itself a sign of malignancy.

C. PARAGANGLIOMA, UNCLASSIFIED. A tumour of the paraganglionic structures that cannot be clearly identified as of the chromaffin or non-chromaffin type.

XI. TUMOURS AND TUMOUR-LIKE LESIONS OF PLURIPOTENTIAL MESENCHYME (MESENCHYMOMAS)

Benign or malignant tumours consisting of two or more clearly identifiable mesenchymal elements in addition to fibrous tissue. The mixed mesodermal tumours of the genito-urinary tract are not included in this group.

XII. TUMOURS OF VESTIGIAL EMBRYONAL STRUCTURES (CHORDOMAS)

Chordoma has been included in the classification because rare examples have been observed in which bone origin could not be demonstrated. Chordoma will be discussed in the volume dealing with tumours of the skeletal system.

¹ Demonstration of intracellular chromaffin granules requires immediate fixation in a chromium salt fixative.

XIII. TUMOURS OF POSSIBLE EXTRAGONADAL GERM-CELL ORIGIN

A. BENIGN

1. *Teratoma [dermoid cyst]*

B. MALIGNANT

1. *Teratocarcinoma*

2. *Embryonal carcinoma*

3. *Choriocarcinoma*

These neoplasms are included because they may occur as primary tumours in the retroperitoneum and pelvis. They will be discussed in the volume on tumours of the urogenital tract.

XIV. TUMOURS OF DISPUTED OR UNCERTAIN HISTOGENESIS

A. BENIGN

A. *Granular cell tumour [granular cell "myoblastoma"]*. A benign tumour of unknown histogenesis made up of large round or polygonal, finely granular, acidophilic cells with small dense nuclei. Superficially located tumours are often accompanied by pseudo-epitheliomatous hyperplasia of the overlying squamous epithelium. Recent evidence speaks against a myoblastic origin.

2. *Chondroma of soft parts*. A benign cartilage-forming tumour that shows no evidence of other cellular differentiation and is unassociated with the skeleton. Some of the smaller examples of this lesion are difficult to distinguish from chondroid metaplasia.

3. *Osteoma of soft parts*. A benign, bone-forming tumour unassociated with the skeleton and showing no evidence of other cellular differentiation. Osseous metaplasia and late stages of myositis ossificans may be difficult to distinguish from this entity.

4. *Nasal glioma [ganglioglioma]*. A malformation consisting of glial tissue occasionally admixed with ganglion cells, occurring as a subcutaneous mass at the base of the nose or as a polypoid lesion attached by a pedicle to the roof of the nasal cavity. The lesion probably consists of cerebral tissue of the frontal lobe growing through a defect in the cribriform

form plate or the ethmoidal bone. A connexion with the brain may or may not be demonstrable at the time of removal. The absence of a fluid-filled space distinguishes the lesion from an anterior encephalocele.

5. *Pacinian tumour*. A still ill-defined benign tumour, probably of neuro-ectodermal origin, containing structures resembling Pacinian corpuscles. Neurofibromas with Meissner-Wagner corpuscle-like structures and blue naevi should be distinguished from this tumour.

6. *Adenomatoid tumour of genital tract*. A benign tumour characterized by irregular gland-like structures or spaces lined or associated with vacuolated mesothelium-like cells. The tumour predominates in the region of the epididymis, spermatic cord, and Fallopian tube, suggesting possible mesonephric origin.

7. *Myxoma*. A benign but often infiltrating growth of unknown histogenesis characterized by rather small inconspicuous round, spindle, or stellate cells within a matrix containing abundant mucoid material, chiefly hyaluronic acid, a loose meshwork of reticulin and collagen fibrils, and scanty vascularity. The large muscles of the shoulder and thigh are the most common sites.

8. *Melanotic progonoma [retinal anlage tumour, melanotic neuroectodermal tumour of infancy]*. A rare benign tumour made up of irregular pigmented melanin-containing cuboidal cells forming nests and alveolar spaces accompanied by a dense fibrocollagenous stroma. The histogenesis is obscure, but the available evidence seems to give strong support to a neural crest origin. The tumour has been observed in the head, mediastinum, shoulder, and testis, as well as in the maxilla.

9. *Fibrous hamartoma of infancy*. A benign and probably hamartomatous growth characterized by an organoid mixture of (1) well-defined trabeculae of dense fibrous connective tissue, (2) whorls or aggregates of loosely arranged stellate or spindle-shaped cells of immature appearance, and (3) mature adipose tissue. The lesion is always located between the epidermis and the superficial fascia and tends to occur in infants between birth and two years of age. The regions of the axilla, the shoulder, and the upper arm are most commonly involved.

B. MALIGNANT

1. *Alveolar soft-part sarcoma [malignant organoid granular cell "myoblastoma"]*.¹ A malignant tumour of unknown histogenesis characterized by small organoid aggregates of polygonal, coarsely granular

¹ The term "malignant non-chromaffin paraganglioma" has sometimes been applied to this tumour, but it is considered undesirable since the etiology is still not clear.

cells surrounded and separated by thin-walled, cleft-like vascular spaces. Typically, many of the cells contain crystalline, diastase-resistant PAS-positive material. This feature helps to distinguish this entity from paraganglioma. The tumour is often mistaken for a metastatic renal cell carcinoma.

2. *Malignant granular cell tumour [malignant (nonorganoid) granular cell "myoblastoma"]*. An exceedingly rare malignant form of granular cell tumour differing from its benign counterpart merely in its slight cellular pleomorphism, its mitotic activity, and its potential to develop metastases.

3. *Chondrosarcoma of soft parts*. An extraskeletal malignant nodular tumour consisting of cords, rows, and nests of chondroblasts within a mucinous matrix rich in sulfated acid mucopolysaccharides. There is evidence that chondrosarcomas of soft parts are less malignant than those that arise from the skeleton. They can be distinguished from mixed tumours of salivary or adnexal origin by the complete absence of glandular or ductal structures.

4. *Osteosarcoma of soft parts*. An extraskeletal malignant tumour composed of atypical mesenchymal cells producing osteoid or bone. The irregular manner of bone formation, as well as the absence of other cellular differentiation, distinguishes the tumour from other forms of sarcoma showing foci of osseous metaplasia. It is important to distinguish this tumour from myositis ossificans and analogous benign bone-forming lesions of soft parts.

5. *Malignant giant-cell tumour of soft parts*. An ill-defined malignant extraskeletal neoplasm of uncertain histogenesis, somewhat resembling a giant-cell tumour of bone. Transitions towards a fibrosarcoma-like pattern have been observed. The tumour is frequently associated with the fascial structures of the thigh. Distant blood-borne metastases are frequent. Superficial atypical fibroxanthomas should not be confused with this entity.

6. *Malignant fibroxanthoma [malignant histiocytoma]*. An ill-defined, usually deep-seated malignant neoplasm probably of histiocytic origin. This tumour shows varying degrees of pleomorphism and is characterized by a focal cartwheel or storiform pattern, multinucleated giant cells of the Touton type, xanthoma cells, siderophages, and nests of chronic inflammatory elements. The collagenous fibrillar ground substance is unevenly distributed and is less abundant than in fibrosarcoma. Metastases may occur. This tumour will be illustrated in the volume dealing with skin tumours.

7. *Kaposi's sarcoma*. A potentially malignant tumour made up of irregular vascular channels and spaces, formed and surrounded by slender spindle-shaped cells with prominent, deeply staining nuclei, superficially resembling leiomyoblasts. The lesions are usually multiple and may occur in the skin as well as in the viscera. Haemosiderin pigment is frequently found. The histogenesis is obscure. The tumour is occasionally associated with malignant lymphoma.

8. *Clear-cell sarcoma of tendons and aponeuroses*. A rare malignant tumour of unknown histogenesis characterized by groups and short fascicles of uniform pale staining, rounded or fusiform cells, with vesicular nuclei and prominent nucleoli. The tumour affects chiefly young adults and tends to be firmly attached to tendons or aponeuroses; it is most common in the foot and knee region of young adults.

XV. NON-NEOPLASTIC OR QUESTIONABLY NEOPLASTIC LESIONS OF SOFT TISSUES, OF INTEREST BECAUSE OF THEIR RESEMBLANCE TO TRUE NEOPLASMS

A. XANTHOMA GROUP

1. *Fibro-xanthoma* [*fibrous histiocytoma*]. A benign, unencapsulated and often richly vascular growth made up of histiocytes and collagen-producing fibroblast-like cells, which are arranged in a whorled or cart-wheel pattern. Frequently, the growth contains lipid-carrying macrophages. It may occur anywhere but is most common in the dermis.

a. *Atypical fibro-xanthoma*. A probably benign growth, which is closely related to fibro-xanthoma but shows a much greater degree of cellular pleomorphism with multinucleate giant cells and occasional giant cells of the Touton type as well as numerous mitotic figures, including atypical forms. The relatively small size of the lesion (generally less than 3 cm), its prevalence in the sun-damaged or irradiated skin of elderly individuals, and the fact that it is usually well-circumscribed, help in the difficult differential diagnosis from malignant fibro-xanthoma (XIV/B/6).

2. *Xanthoma*. A benign growth made up chiefly of xanthoma cells (lipid-carrying histiocytes), occasional Touton-type giant cells, and varying amounts of fibrous connective tissue. The lesion may be solitary or multiple and is often associated with high levels of serum cholesterol and phospholipids (hypercholesteraemic xanthomatosis).

3. *Juvenile xanthogranuloma* [*naevoxanthoendothelioma*]. A benign cellular growth of childhood occurring as a tan-to-brownish nodule in the skin and deeper tissues, principally of the head, neck, and trunk. Characteristically, the lesion consists of a mixture of small, often lipid-bearing oval or spindle-shaped cells, presumably histiocytes, Touton-type giant cells and, in the superficial lesions, occasional eosinophils. The lesion is self-limiting and in the majority of cases disappears spontaneously. It is not known to be associated with elevated serum lipid levels.

4. *Retroperitoneal xanthogranuloma* (*Oberling*). A mixture of xanthoma cells, acute or chronic inflammatory elements, and varying amounts of fibrous connective tissue occurring as an infiltrating tumour-like lesion in the retroperitoneum. Lesions of similar histology may also occur at other sites. Xanthogranulomatous pyelonephritis may mimic the picture of a retroperitoneal xanthogranuloma. Differential diagnosis from liposarcoma may be exceedingly difficult.

5. *Nodular tenosynovitis* [*giant cell tumour of tendon sheath*] and *pigmented villonodular synovitis*. A slowly growing localized or diffuse process composed chiefly of histiocyte-like stroma cells, with or without deposits of haemosiderin, xanthoma cells, and multinucleated giant cells. Collagen is a constant feature of the lesion but variable in amount. The process may arise from either tendon sheaths or the synovial membrane of joints. It most commonly affects the fingers and the knee. Erosion of the underlying bone is occasionally observed.

B. *GANGLION*. A more or less cystic, fluid-filled lesion, possibly resulting from mucoid degeneration of collagen. The lesion is frequently associated with aponeuroses or tendons, but seldom communicates with synovial cavities. The cystic space is not lined by synovial cells. The non-cystic parts of a ganglion may bear a close resemblance to a myxoma.

C. *LOCALIZED MYXOEDEMA*. A tumour-like dermal accumulation of hyaluronidase-sensitive mucinous material, frequently but not always associated with thyroid dysfunction.

D. *MYOSITIS OSSIFICANS*. A benign, pseudo-neoplastic, reactive process made up of a mixture of collagen-producing, cellular, fibrous connective tissue and osteoblastic tissue engaged in orderly osteoid and bone formation. Characteristically, the formation of mature bone is most prominent in the periphery of the lesion, and this is the main criterion for differentiation from an osteosarcoma. Mitotic figures are frequent. About half the cases give a history of preceding trauma.

3. PROLIFERATIVE MYOSITIS. A rapidly growing, poorly circumscribed, probably reactive proliferation of fibroblasts and ganglion-cell-like giant cells involving chiefly the connective tissue framework of striated muscle tissue. In contrast to myositis ossificans, a history of preceding trauma is infrequent and the lesion occurs chiefly in patients older than 45 years. The lesion is benign and should not be mistaken for a rhabdomyosarcoma or some other malignant neoplasm.

XVI. SOFT-TISSUE TUMOUR, UNCLASSIFIED

Any primary tumour of soft tissue that cannot be placed in one of the categories described above.

Abbreviations used in the captions to the colour photomicrographs reproduced on the following pages:

H & E: Haematoxylin-eosin
 AMP: Colloidal iron (acid mucopolysaccharides)
 PTAH: Phosphotungstic acid haematoxylin
 PAS: Periodic acid Schiff reaction

The code references on the right-hand side refer to the various categories of the histological classification given on pages 19-25.



Fig. 1. Fibroma molle

Female, scapular region
 No recurrence (4-year follow-up)

I/A/2

H & E

x 100

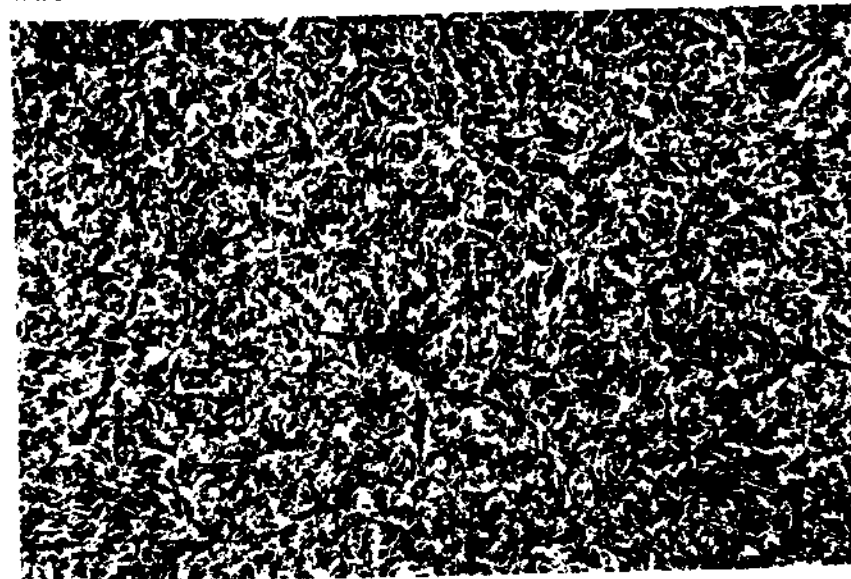


Fig. 2. Dermatofibroma

Female, 27 years, shoulder region
 No recurrence (5-year follow-up)

I/A/3

2, 3, 7, 8 - TCDD BODY BURDEN DETERMINATION

PROTOCOL FOR

SERUM DIOXIN (2,3,7,8 - TCDD) TESTING

Testing for serum dioxin levels is a highly technical and exacting procedure with at least the following requirements:

- Standardization and quality control in the collection, processing, and shipping of specimens; and
- Specialized laboratory facilities for measurement of serum TCDD levels (i.e., High Resolution Gas Chromatography/High Resolution Mass Spectrometry or HRGC/HRMS).

These two major areas of specimen collection processing and laboratory measurement will be discussed.

1) Specimen Collection and Processing

Two major issues must be addressed in the collection and processing of blood specimens for serum dioxin (TCDD) testing: a) the amount of blood required for the assay, and b) the necessity of standardization and quality control of procedures.

At the present time, given the state of the science for dioxin testing, one (1) unit of blood is required for the assay (see Patterson et al, 1987 for discussion). The requirement for this amount of blood places constraints on how it will be obtained. Blood must be collected by trained personnel, working under the direction of a qualified, licensed physician. The donor must be monitored and never left unattended during or immediately after the collection of the blood. Further, pre-collection screening must include a medical history to rule out hepatitis, AIDS, or other serious illnesses, and a physical exam to determine the temperature, pulse, blood pressure (below 180/100 is acceptable) and hematocrit (41 is acceptable for males and 38 for females.) These requirements for safe collection of the blood specimen rule out an in-home collection protocol even using trained personnel.

Further requirements for standardization and quality control of specimen processing and shipping also rule out an in-home protocol. Specific specimen processing and shipping requirements include:

- collection bags must have no anti-coagulant;
- blood-pack must be allowed to clot at room temperature for 3 hours before spinning to separate serum;
- blood-pack must be spun down, using a Beckman Centrifuge Model #J-6M or equivalent; at 4,000 RPM for 10 minutes at 4 degrees C.
- serum is then transferred into a 300 ml transfer pack using a "Plasma Extractor";
- serum is again centrifuged as above and transferred to (4) Wheaton bottles using a plasma transfer set;
- serum samples are stored at -20 degrees C or less until shipment; and
- samples are labeled according to specifications and shipped on dry ice to the laboratory via a 24-hour delivery service (e.g., Federal Express).

The full CDC protocol and specifications are attached. These very specific requirements for processing of specimens prior to shipment necessitate collection at central sites where processing and preparation for shipment could be carried out.

A feasible and already tested system for specimen collection, processing, and shipment is to contract for service with the Red Cross. Most importantly, the Red Cross is currently performing this work for the Ranch Hand Study, is aware of the special requirements and the necessity for standardization and quality control, and has been performing satisfactorily according to CDC specifications. Further, Red Cross personnel are qualified and appropriately supervised for collection of a unit of blood and have the equipment and facilities for the required processing and shipment of the serum specimens.

Contact with Ms. Natalie Gerace of the National Red Cross, Blood Operations Support Office indicated that the organization was willing and able to perform this work for the proposed study. Since the subjects for dioxin testing will most likely be dispersed throughout the country, it will be necessary to arrange for blood collection at a potentially large number of Red Cross offices. Ms. Gerace indicated that this could be arranged through service contracts with the regional offices (up to 56 service contracts may be required depending on geographic location of the subjects).

In addition to negotiating service contracts, training of the Red Cross personnel in the special requirements of specimen collection, processing and shipping will be necessary to ensure standardization of procedures. Training of personnel at the

three Red Cross sites for the Ranch Hand Study was provided by CDC personnel from the Special Activities office. Brenda Lewis from this office indicated that CDC would prefer and would be available to provide this training of Red Cross personnel for the proposed study.

However, unlike the Ranch Hand Study, use of a large number of collection sites is anticipated. Two alternatives for training personnel were considered:

- 1) providing centralized training at selected regional sites across the country; or
- 2) training several technicians who would, in turn, provide training at local collection sites.

Because it is necessary to train all personnel who will be involved in any aspect of the protocol, and because several people may be involved at any one site, the first alternative is not feasible. Further, it has been CDC's experience that on-site training is most effective.

Therefore, a "train the trainer" technique is proposed. A number of Red Cross technicians (number to be determined by the number of collection sites required) will be trained and evaluated by CDC staff from the Special Activities Office. These technicians will then train the local Red Cross personnel on-site, using the CDC protocol. To ensure standardization and quality control, it is further proposed that CDC personnel make on-site visits to randomly selected local collection sites to monitor implementation of the protocol during the course of the specimen collection period.

2) Serum Assay

At the present time CDC has the only laboratory in the country capable of carrying out the serum dioxin assay. Housed in the Division of Environmental Health Laboratory Sciences, Center for Environmental Health, the Toxicology Branch has made its own analytical standards to provide an accuracy base for the assay, has three high resolution mass spectrometry machines, has programmed and debugged the system, and has established thorough quality control procedures. Since CDC is currently performing serum assays for TCDD and since it would take at least a year to set up a laboratory in another facility, it is both time- and cost-efficient to use CDC laboratory for the assays for the proposed study.

A detailed description of the assay is contained in the attached article by Patterson et al (1987) and therefore is not repeated here. An assay on an individual specimen takes 1 1/2 days to complete. Throughput is slow, related to the complex cleaning required for each specimen. At maximum capacity, CDC could complete 75 assays per week and more reasonably 60 assays per week.

RANCH HANDS PILOT STUDY
FOR SERUM DIOXIN
CASE 87-0006

DIVISION OF ENVIRONMENTAL HEALTH AND LABORATORY
SCIENCES
CENTER FOR DISEASE CONTROL

Prepared: 11/14/86

RANCHHAND PILOT STUDY
FOR SERUM DIOXIN ANALYSIS

I. PREPARATION OF WORK AREAS

A. Materials Needed Per participant

1. 15% aqueous soap swab
2. 10% acetone in 70% alcohol (1:9) swab
3. Tincture of iodine solution swab
4. Gauze, sterile, individually wrapped, 4"x4"
5. Tourniquet
6. 500 mL blood bag WITHOUT anticoagulant (Travenol)
7. Fenwal centrifuge bag
8. 300 mL transfer pack (Travenol)
9. Plasma extractor
10. Plasma transfer set (Travenol)
11. Hand scale or vacuum assist device
12. Clamps
13. Hemostats
14. Pliers
15. Preprinted labels

II. COLLECTION OF BLOOD

*****VERY IMPORTANT:***** Blood collection for serum differs in two ways from standard blood collection for plasma.

1. Collection bags must have NO anti-coagulant.
2. The blood-pack must be allowed to clot at room temperature for 3 hours before spinning to separate serum.

A. Introduction

Blood shall be collected from donors by trained personnel, working under the direction of a qualified, licensed physician. The donor shall never be left unattended during or immediately after collection of blood. Blood collection must be made by aseptic methods, utilizing a sterile closed system, and a single venipuncture. If more than one skin puncture is needed, another container and donor set must be used.

B. Preparing Venipuncture Site

1. Blood should be drawn from large firm vein in area free from skin lesions.
2. Apply tourniquet, select vein.

3. Release pressure, prepare skin site.
 - a. Scrub with 15% aqueous soap or detergent for 30 seconds.
 - b. Remove soap with 10% acetone in 70% alcohol (1:9) and allow to dry.
 - c. Apply tincture of iodine solution and allow to dry.
 - d. Remove iodine with acetone/alcohol mixture and allow to dry.
 - e. Cover the site with dry sterile gauze until ready to perform venipuncture. After skin has been prepared, it must NOT be touched again.

C. Unit Collections (Large Volumes)

IT IS IMPERATIVE THAT THE PHLEBOTOMY BE PERFORMED INTO BLOOD-PACKS WITHOUT ANTICOAGULANT.

1. Check bag without anticoagulant for defects.
2. Bag may be gravity filled or vacuum filled. If gravity filled, use a hand scale to monitor volume; if vacuum filled, a vacuum assist device is used.
3. The bags should be affixed with the label showing the participants ID number and identified "Blood Collection Bag".
4. Select vein. Prepare skin site. Reapply tourniquet.
5. Remove cover from needle. Do venipuncture immediately.
6. Open tubing. If using vacuum assist device, turn on.
7. Tape tubing to hold needle in place.
8. Fill to desired amount. Release tourniquet.
9. Remove needle from arm. Cover with gauze. Apply steady pressure for about 15 minutes.
10. Check arm, apply bandage when bleeding stops.

D. Care of Donor

1. Have donor recline in donor chair under close observation.
2. After a few minutes, allow donor to sit up.
3. If there is any adverse reaction to giving blood, the blood bank physician should be notified immediately.
4. At the first sign of adverse reaction during phlebotomy, remove tourniquet, and withdraw needle from arm.

III. PROCESSING BLOOD

A. Processing Units

LET THE BLOOD-PACK CLOT AT ROOM TEMPERATURE AT LEAST 3 HOURS BEFORE SPINNING.

1. Use Beckman Centrifuge Model #J-6M or equivalent.
2. Place bag containing blood into Fenwal Centrifuge bag. A collection bag filled with water is used for balancing if only one bag of blood is processed.
3. Spin bags at 4000 RPM for 10 minutes at 4 °C.
4. Transfer serum into 300 mL transfer pack using a "Plasma Extractor".
5. Clamp tubing with 2 clamps about 1 inch apart. Cut between clamps.
6. Repeat steps 2 through 5.
7. Using the preprinted labels provided, label each of the Wheaton bottles as follows:

<u>Size/Type Bottle</u>	<u>Bottle Label</u>
4 oz Wheaton bottle	87-0006-0001-S1-Serum Dioxin
4 oz Wheaton bottle	87-0006-0001-S2-Serum Dioxin
6 mL Wheaton bottle	87-0006-0001-S3-Lipid Profile
10 mL Wheaton bottle	87-0006-0001-S4-Serum Reserve

8. Use a plasma transfer set to transfer serum to Wheaton bottles.
 - a. Insert the sharp end into one of the outlet ports in top of the bag.
 - b. Close tubing with thumb roller on tubing.
 - c. Press bag with "Plasma Extractor".
 - d. Hold open end of tubing over open pre-labeled Wheaton bottles.
 - e. Open tubing and put 5 mL in "S3" bottle, 10 mL in "S4" bottle and divide the rest into the 4 oz bottles.
 - f. Extract only the serum being careful that cells do not enter the bottle.
 - g. Log in the serum samples and store at -20 °C or less until shipment.

IV. SHIPMENT OF SPECIMENS TO CDC, ATLANTA, GA

A. Beginning of Study and General Instructions

1. Maintain a supply of dry ice from a local supplier for transporting specimens to CDC. A block should be sawed at the plant into 1" slabs. Then each of these should be sawed lengthwise. A 7"x10" slab would fit easily into the shipper without having to break the slab. (Large pieces are preferable to small chunks, since they do not volatilize as rapidly.)
2. For all shipments, do not pack shippers with frozen specimens and dry ice until just before shipment.
3. Telephone the laboratory at CDC the day the shipment is transported (404) 454-4300. Speak with Brenda Lewis.

B. Specimen Shipping List

1. For each shipment, fill out a blank Specimen Shipping List provided by CDC. If the number of specimens in a shipment is too large to fit on one page, please use the continuation sheets provided. Please give the following information on the blank shipping lists. (See attached example of a completed Specimen Shipping List.):
 - Page number - e.g. 1 or 4
 - Shipment Number - number shipments sequentially starting with 1
 - Number frozen shippers - total number of shippers (containing frozen serum specimens) which are in this shipment
 - Type of Specimen - serum
 - Number of Specimens - number of each type of specimen shipped
 - Name, title, signature, and phone number of person sending shipment or initials as indicated on the continuation sheets
 - Date shipped
 - Specimen ID for each participant - e.g., 87-0006-0011
 - For each participant, check (✓) each individual specimen type/aliquot included in this shipment
 - Date Collected - e.g., 111886
 - Comments - Specify any deviations from collection, storage, and shipment protocols, and date of occurrence

C. Frozen Specimens

1. Materials needed per shipper

- 1 styrofoam shipper (each shipper will hold frozen specimens from approximately 1 participant)
- 3-4 lbs. dry ice
- 4 bubble-pack bags 4"x7"
- Safety glasses or eye shield
- Strapping tape
- Gloves for handling dry ice and frozen specimens
- Sheets of bubble-pack packing material
- CDC "Specimen Shipping List" filled out
- Zip-lock bag
- Frozen serum specimens (4 serum bottles per participant)

2. Packing procedure

- When packing the shippers, use gloves to handle the dry ice to avoid burning the hands. Glasses or an eye shield should also be worn if the dry ice cakes are to be broken into small pieces.
- Place a frozen serum specimen from each participant in one 4"x7" bubble bag and seal.
- Pack 1 set of filled bubble bags upright in the bottom of the shipper. If necessary, use sheets of bubble-pack, packing material to ensure the specimens vertical position.
- Put one layer of sheet bubble-pack material on top of the specimens.
- Fill the shipper with dry ice:
- Insert the completed "Specimen Shipping List" in a 12"x12" zip-lock bag and secure to the top of the polyfoam lid with filament tape.
- Secure the outer carton lid on the shipper with filament tape.

3. Shipping Procedure

- Cover or remove previous address labels on all shippers.
- Label each shipper with the following:

Preadressed "FEDERAL EXPRESS" mailing label with the following address:

Brenda Lewis
Chamblee, Building 32, Room 1502
Centers for Disease Control
4770 Buford Highway
Chamblee, GA 30341

HUMAN BLOOD - THIS SIDE UP label

DRY ICE label

ORM-A written on the box

- Call the Federal Express office at 1-800-238-5355 to arrange for pick-up. Federal Express requires a one-hour notice before the needed pick-up.
- Telephone the laboratory at CDC the day the shipment is mailed (404) 454-4300. Speak with Brenda Lewis or Sue Lewis.

RANCHLAND PILOT STUDY

87-0006

SERUM COLLECTION AND PROCESSING

600mL BLOOD-PACK UNIT
WITHOUT ANTICOAGULANT

LET CLOT AT ROOM
TEMPERATURE AT LEAST
THREE HOURS

SPIN AT 4000 RPM AT 4°C
FOR TEN MINUTES

TRANSFER SERUM TO A TRANSFER PACK

SPIN AT 4000 RPM AT 4°C
FOR TEN MINUTES

ALIQOT
INTO DESIGNATED BOTTLES

S1
(4 oz. BOTTLE)

S2
(4 oz. BOTTLE)

S3
(6mL WHEATON)

S4
(10mL WHEATON
BOTTLE)

ADD 100mL

ADD 100mL

ADD 5mL

ADD 10mL

FREEZE IMMEDIATELY AT -70° C
AND STORE AT SAME TEMPERATURE
UNTIL SHIPMENT TO CDC ON DRY ICE

SPECIMEN INFORMATION SYSTEM
 FORM 1 - BANGOR AND PLYMOUTH
 SPECIMEN SHIPPING LIST FOR BLOOD SPECIMENS

CASE NUMBER

87-0006

SHIPMENT NUMBER

SHIPMENTS

TITLE

NAME

SHIPPED BY

SIGNATURE

DATE SHIPPED

PHONE NO.

NO. SPECIMENS

RECEIVED BY

NAME

CDC UNIT

OF

SIGNATURE

DATE RECEIVED

SPECIMEN ID

TYPE/ALiquot NO.

DATE

COMMENTS: SPECIFY ANY DEVIATION FROM COLLECTION,
 STORAGE, AND SHIPMENT PROTOCOLS, AND DATE OF

87-0006-XXXX

S1 S2 S3 S4

MH-DD-YY
 XX-XX-XX

87-0005-

87-0005-

87-0005-

87-0005-

87-0005-

87-0005-

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*TYPE OF SPECIMEN

High-Resolution Gas Chromatographic/High-Resolution Mass Spectrometric Analysis of Human Serum on a Whole-Weight and Lipid Basis for 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin

Donald G. Patterson, Jr.,* Larry Hampton, Chester R. Lapeza, Jr., William T. Belser, Vaughn Green, Louis Alexander, and Larry L. Needham

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We describe an analytical method to measure 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) and other TCDD isomers in human serum; the method uses a highly specific cleanup procedure and high-resolution gas chromatography/high-resolution mass spectrometry. The 2,3,7,8-TCDD is quantified by the isotope dilution technique with [¹³C₁₂]-2,3,7,8-TCDD as the internal standard. Other TCDD isomers are estimated by using published relative response factors. The 1.25 part-per-quadrillion (ppq) limit of detection for 200-g samples is more than adequate for determining 2,3,7,8-TCDD concentrations in human serum specimens. The method is modified for analyzing 50-g and 10-g serum samples. Analytical accuracy is demonstrated by the results obtained in analyzing spiked samples. The method is shown to be unaffected by a number of potentially interfering compounds. A series of quality control material is used to verify system performance. For 200-g samples containing 25.8 ppq of native 2,3,7,8-TCDD, a coefficient of variation (CV) of 13.0% is observed ($n = 20$). For 10-g samples from a pool fortified with 2,3,7,8-TCDD (1.9 parts per trillion, $n = 22$), a CV of 15.5% is observed.

Intense public health interest continues to focus on the polychlorinated dibenzo-*p*-dioxins and related compounds. Humans are exposed to many of these compounds from such sources as municipal incinerators (1) and automobile exhausts (2); other sources, such as the manufacture and use of compounds for which 2,4,5-trichlorophenol is a synthetic intermediate, give rise primarily to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD). The 2,3,7,8-TCDD congener, one of 22 tetra isomers, reportedly is the most toxic of these compounds. Studies have documented its toxicological properties, such as acute oral LD₅₀ (3), teratogenicity (4), carcinogenicity (5), and fetotoxicity (6) in selected animal species. However, human toxicity associated with exposure to 2,3,7,8-TCDD has not been as well documented. Findings of a recent study of the residents of a mobile home park in Missouri suggested that long-term exposure to 2,3,7,8-TCDD is associated with depressed cell-mediated immunity, although the effects did not result in an excess of clinical illness (7). However, in this study of health effects and in another (8), exposure was derived from self-reported histories and not from body burden measurements. Such measurements are needed in these health-related studies.

Polychlorinated dibenzo-*p*-dioxins are lipophilic and thus are found in body stores that are high in lipid content. Body burden measurements for 2,3,7,8-TCDD in humans have been determined in blood plasma (9), in human milk (10, 11), and in adipose tissue (12-15). The primary disadvantage of the breast milk matrix in health-related studies is that the cohort is restricted to females within a limited age range. The primary disadvantage of adipose tissue is that the sample must be obtained surgically. Therefore, a biological specimen, such as blood or its components, that can be obtained with a less invasive procedure than adipose and that is available from all participants, is highly desirable.

Other lipophilic xenobiotics, such as the chlorinated hydrocarbon pesticides and polychlorinated biphenyls, have been determined in both human adipose tissue and serum for years. Because the fat content of serum is much less than that in adipose tissue, these compounds are in higher concentrations in the adipose tissue. Consequently, a large volume of serum

is normally used when these compounds are determined in humans. Because 2,3,7,8-TCDD is present at the picogram-per-gram or parts-per-trillion (ppt) level in adipose tissue, any method for determining it in whole blood, plasma, or serum would have to be particularly sensitive as well as selective. These criteria require methods based on gas chromatography/mass spectrometry (16). We report here a high-resolution gas chromatographic/high-resolution mass spectrometric method for determining 2,3,7,8-TCDD in human serum; this method is an adaptation of our method for determining this xenobiotic in human adipose tissue (17, 18).

EXPERIMENTAL SECTION

Safety. Chemists undertaking this work with 2,3,7,8-TCDD and other such toxic compounds must understand the potential health effects of such compounds (19) and prudent laboratory practices for handling toxic chemicals (20). Specific precautions have been described (21, 22). More recent Environmental Protection Agency (EPA) draft methods have emphasized specific aspects of protective equipment, training, personal hygiene, isolation of the work area, disposal of waste, laboratory cleanup, laundry, wipe testing, problems in inhalation, and accidents. We have described safety precautions in the operation of our Chemical Toxicant Laboratory (23), and other laboratories have also described their procedures (24).

Materials. In addition to the materials already described (17, 18), we used ethanol (anhydrous reagent, J. T. Baker, Phillipsburg, NJ), ammonium sulfate (certified primary standard, Fisher Scientific Co., Fair Lawn, NJ), and sulfuric acid (Reagent ACS, Fisher Scientific, Fair Lawn, NJ).

Sample Preparation. Two hundred grams of serum is weighed into a 500-mL Teflon bottle (Nalge Co., Rochester, NY). An internal standard solution consisting of 240 pg of ^{13}C -labeled 2,3,7,8-TCDD is added to the sample. The standard (maintained at room temperature) is accurately measured by using an electronic digital pipet (Rainin Instrument Co. Inc., Woburn, MA) with disposable microliter pipet tips. The disposable pipet tip is primed by dipping the tip 2-3 mm below the surface of the standard and operating the pipet for pickup and dispensing back into the standard. A repeat operation is done for pickup and dispensing into the side of the bottle containing the 200 g of serum. The sample is capped tightly and shaken vigorously with a wrist action shaker Model 75 (Bunnell Corp., Pittsburgh, PA) for 30 min. To the sample is then added 100 mL of aqueous saturated ammonium sulfate solution (50 mL to a 10- to 50-g sample), 100 mL of absolute ethanol (50 mL to a 10- to 50-g sample), and 100 mL of hexane (50 mL to a 10- to 50-g sample). The flask is then capped tightly and shaken vigorously for 30 min with the wrist action shaker. The emulsion formed after shaking is centrifuged for 10 min at 1500 rpm. The top hexane layer is transferred to a 500-mL Teflon separatory funnel. To the bottom aqueous layer is added another 100 mL of hexane, followed by vigorous shaking, centrifuging, and combining of the two hexane extracts. The combined hexane extracts (200 mL) are then extracted with concentrated sulfuric acid with a 500-mL separatory funnel and a total of 200-mL of concentrated sulfuric acid (70 mL for 10- to 50-g samples) in 20-mL aliquots. The first three extractions are not shaken vigorously to prevent the formation of an emulsion. The acid-washed hexane is then extracted with a total of 75 mL of deionized water in 25-mL aliquots. The hexane is then transferred to a 250-mL Erlenmeyer flask, followed by the addition of 10 g of sodium sulfate and evaporation under a nitrogen stream to ~75 mL. The sample is then loaded onto the first chromatography column for part I of a two-part sample cleanup procedure (17, 18), which is capable of processing five samples unattended overnight.

The sample from part I in toluene is then subjected to rotary evaporation at 55 °C under ~0.1-0.2 atm vacuum after 50 μL of dodecane (99%, Aldrich Chemical Co., Inc., Milwaukee, WI) is added. The toluene solution is carefully taken to about 1 mL and then blown to dryness under a gentle stream of nitrogen. After the sample is reconstituted in hexane, it is ready for part II of the procedure (17). Before evaporation of the final extract to dryness, 1 μL of dodecane is added to the conical sample vial. This sample extract is reconstituted to 5 μL with toluene just before analysis by high-resolution gas chromatography/high-resolution mass spectrometry (17). 15

Instrument Analysis. Our analytical instrument system consists of a VG ZAB-2F high-resolution mass spectrometer with a VG 2250 data system and a Hewlett-Packard 5840 gas chromatograph. Our analyses are conducted in an isomer-specific mode, with a 60 M SP2330 capillary column. The injection is splitless with a 30-s purge. The injector temperature is 240 °C. The initial column temperature of 100 °C is held for 2 min, programmed to 250 °C at 15 °C/min, and held for 14 min. The average linear velocity of helium is 23 cm/s or about 2.9 mL/min flow rate. The mass spectrometer is operated in the high-resolution (static RP = 10000 at 10% valley) selected ion recording mode, with perfluorotributylamine used to provide a lock mass at m/z 314. Peak top jumping is accomplished by stepping the accelerating voltage after any necessary correction during the scan of the lock mass. Ions m/z 320 and 322 provide a measure of the native TCDD, and ions m/z 332 and 334 are monitored for the elution of the labeled internal standard. Five analytical standards that correspond to 1.25-25 ppq of 2,3,7,8-TCDD in a 200-g serum sample have been used to establish a linear calibration curve. The data for the standard curve are tabulated in Table I. The internal standard is the $^{13}\text{C}_{12}$ -2,3,7,8-TCDD at a concentration corresponding to 1.2 ppt in the original 200-g samples. The other TCDD isomers can be quantitated by using our published (25) response factors relative to 2,3,7,8-TCDD. The best precision in quantitation is obtained by using chromatographic peak areas and by using the sum of the two ions for the native TCDD and two ions for the internal standard.

On a regular basis, isomer-specific chromatography is demonstrated by analyzing a standard containing the 22-TCDDs. Our serum Quality Control (QC) pools L and H contain, among other dioxins and furans, the 1,2,3,7,8-TCDD isomer that can be used to establish isomer specificity for 2,3,7,8-TCDD in analytical runs containing a sample from these QC pools (see Figure 1). The calibration curve is verified by analyzing an analytical standard during an 8-h shift. Instrument resolution at 10000 RP, tuning, and other parameters are checked on a regular basis to ensure optimum sensitivity and specificity. Criteria for a positive TCDD determination are as follows: (1) signal/noise greater than 3/1 for both signals on ions 320 and 322; (2) signal/noise greater than 10/1 for both signals on ions 332 and 334 from the internal standard; (3) observed retention times within ± 1 scan of each other on ions 320 and 322 and the relative retention time (RRT) (to $^{13}\text{C}_{12}$ -2,3,7,8-TCDD) must be within 2 part-per-thousand of the RRT of the analytical standard; (4) the ratio of the intensities of the ion 320 to 322 and 332 to 334 is within the 95% confidence intervals established for these ratios (see Table II).

Spiked and nonspiked human serum QC material has been prepared and characterized. Incorporating these materials in the analytical run sets control limits and provides a means for demonstrating that the analytical system is in control. Recovery data are calculated on the basis of the absolute (are) counts for m/z 332 + 334 in the sample vs. the standards.

Serum Total Lipids. Cholesterol esters, triglycerides, and high-density lipoprotein cholesterol (HDL) are determined in duplicate by standard methods (26). Total phospholipids are determined in duplicate by a modification (27) of the Folch procedure (28). Free cholesterol is determined in duplicate by an enzymatic method (29). The summation method (30) estimates total lipids in serum. The agreement is excellent between this summation value and the corresponding estimate obtained through extraction and gravimetric analysis (30).

QUALITY ASSURANCE (QA) PROGRAM

Quality Control (QC) Materials. The main feature of the QA program is the use of matrix-based materials that are well characterized for TCDD concentration to ensure that the analytical system is in control. Human serum has been dispensed into various sized aliquots. Two of the pools have been spiked with various levels of dioxins and furans, whereas the other pool has not been spiked. Three pools of material are available to be inserted into the analytical run. The spiked pools contain the following dioxins and furans in addition to those already present in human serum: 2,3,7,8-TCDD; 1,2,3,4-TCDD; 1,2,3,7,8-pentachlorodibenzo-*p*-dioxin (PnCDD); 1,2,4,7,8-PnCDD; 1,2,4,6,7,9-hexachlorodibenzo-*p*-dioxin (HxCDD); 1,2,3,6,7,9-HxCDD; 1,2,3,6,7,8-HxCDD; 1,2,3,7,8,9-HxCDD; 1,2,3,4,7,8-HxCDD; 1,2,3,4,6,7,9-heptachlorodibenzo-*p*-dioxin (HpCDD); 1,2,3,4,6,7,8-HpCDD; octachlorodibenzo-*p*-dioxin (OCDD); 2,3,7,8-tetrachlorodibenzofuran (TCDF); octachlorodibenzofuran (OCDF).

QC Charts. QC Charts graphically document the analytical performance of the system. Figure 2 shows the QC chart for pool L, which was established during the development of this method; the statistical data are shown in Table II.

Details of the Analytical Run. The status of the specimens being analyzed is unknown to the laboratory analysts. Samples are received and arranged in analytical runs of five (three serum samples, a method blank, and one QC sample from pool I or L). In every fourth analytical run, a QC sample from a different pool is substituted for the pool I or L QC sample. In addition, a serum sample selected at random from one of the four analytical runs will be analyzed in duplicate, providing that sufficient serum is available. The samples are then submitted for cleanup by a manual method (17) or an automated procedure (18) and then submitted to the mass spectrometry (MS) laboratory for analysis. The MS personnel are also unaware of the nature of the extract.

To minimize the possibility for carryover or cross-contamination of samples and analytical standards, analysts use separate syringes for samples and for each analytical standard. The sample syringe is discarded periodically or when a serum sample that contains more than 75 ppq of 2,3,7,8-TCDD is analyzed. Between injections of a standard or a sample, the syringe is inserted through a Teflon-coated septum into a 15-mL vial containing 12 mL of toluene, and the barrel is filled and emptied 10 times. This process is repeated twice more with different 15-mL vials containing toluene. A final wash of the syringe is done by filling and emptying the barrel 10 times with a fourth toluene wash solution. These wash solutions are discarded at the end of each working day. The final 5 μ L of toluene for reconstituting samples is then taken from a fifth verified blank toluene source. The step-by-step procedure leading to an analytical result, the accompanying documentation, and the criteria for identifying TCDD and for reporting results have been reported previously (17).

EVALUATION AND VALIDATION STUDIES

Interferences. We have previously described (17) our studies to verify the elimination, by the cleanup process, of compounds that could interfere in the analysis for TCDDs. The results of these analyses indicated that these potentially interfering compounds, which are present at 10^3 - to 10^6 -fold excess, are effectively removed during the multicolumn cleanup of the sample.

Validation of 2,3,7,8-TCDD Analytical Standards. In a previous analysis of a series of 2,3,7,8-TCDD standards received from various laboratories and chemical suppliers, we found that the stocks varied from -65% to +35% of the stated concentration (17). Because of these findings, we validated our stock solution against 2,3,7,8-TCDD that we had synthesized and characterized in our laboratory. At the time of the previous report, the National Bureau of Standards (NBS) had plans to issue a Certified Reference Material for 2,3,7,8-TCDD, which is now available. Therefore, we have validated our stock standard solution that we used for our quantitative measurements against CDC synthetic material and EPA and NBS analytical standards. The results of the measurements are given in Table III. The agreement among these standards is very good and well within the stated uncertainty.

Recovery of 2,3,7,8-TCDD. Human serum samples (200 g, 50 g, 10 g) were spiked with 240 pg of [$^{13}\text{C}_{12}$]-2,3,7,8-TCDD and processed through the entire cleanup procedure described above and the entire five-column cleanup described previously (17, 18). These samples were analyzed by using [$^{37}\text{Cl}_4$]-2,3,7,8-TCDD as the external standard to give average recoveries of 69%, 54%, and 68%, respectively (Table IV).

Recovery of the 22 TCDDs. A standard that contained the 22-TCDDs that had been processed through the five-column cleanup procedure was compared with a standard analyzed directly by GC/MS. The results, which ranged from 95% to 124% recovery (17), were adequate for quantitating the 22 TCDDs.

Within-Vial Variability. Periodically, we need to rerun the mass spectral analysis of a sample because of a number of possible hardware or software problems such as electrical failure in the laboratory, poor signal-to-noise ratio, incorrect isotope ratios, high-voltage shut down, or data system crash. In addition, highly concentrated samples may sometimes saturate the detector and require dilution before a second analysis. We have examined the variability involved in a reanalysis from a sample vial (2 μ L of 3 μ L) that was analyzed (2 μ L of 5 μ L) the same day, one day earlier, and up to 27 days earlier (Table V). The data in Table V indicate that the samples may be reanalyzed up to a month later with less than a 10% bias being introduced.

Method Performance. All 200-g serum samples examined thus far have produced sufficiently strong signals (signal-to-noise ratio $> 3/1$) to permit quantification. With regular routine maintenance, a limit of quantification of 5 ppq for a 200-g sample may be readily achieved for routine samples from epidemiological studies. We have previously defined our criteria (17) for reporting samples such as Q (quantifiable), NQ (nonquantifiable), and ND (nondetect). The accuracy of the method is demonstrated in part by the spiked recovery experiments (Table IV). In these tests, three different calibrated aliquots of 2,3,7,8-TCDD were spiked into separate 200-g samples of pool I. This experiment was performed twice by two different analysts. The values obtained on analysis are in good agreement with the expected values. We have also conducted a series of experiments in which we combined vials of QC pool L to provide ~20-, 30-, and 40-g samples that were spiked with 240 pg of $^{13}\text{C}_{12}$ -2378-TCDD and carried through the analytical procedure. The expected and observed values (Table VI) are in good agreement. Another measure of system performance is the precision associated with characterizing the QC materials (see Table II). For spiked 10-g serum samples at the 1.9 ppqr level, a coefficient of variation (CV) of 15% was observed. For 200-g unspiked serum samples at the 25.8-ppq level, a CV of 13% was observed.

Stability of 2,3,7,8-TCDD in Human Serum. Samples of QC pools I and L were stored at -40°C and analyzed at various times during the method development phase of this study. We have observed no apparent degradation of the 2,3,7,8-TCDD in these materials over a period of 1 year.

RESULTS AND DISCUSSION

Human Serum Results. During and after the method development phase of this study, we have successfully analyzed, for 2,3,7,8-TCDD, various individual samples of human serum, plasma, and whole blood, as well as pooled samples collected from local and regional centers. These results, summarized in Table VII, are the first reported levels of 2,3,7,8-TCDD in human serum taken from individuals in the general population with no known exposure to 2,3,7,8-TCDD. The arithmetic mean of the individual serum samples is 47.9 ppq (range of 13.5–211 ppq, $n = 22$) on a whole-weight basis and 7.56 ppqr (range of 1.87–26.0 ppqr, $n = 21$) on a lipid-weight basis. These results in serum on a lipid-weight basis are in good agreement with results that we have published previously (14, 15, 17) relating to human adipose tissue, as well as with results in adipose tissue from other laboratories (12, 13, 31–33) as shown in Table VIII.

Future Method Development. A key to substituting serum for the more difficult to obtain adipose specimen is to experimentally calculate the partitioning coefficient of 2,3,7,8-TCDD in these two matrices. We have begun a study of the distribution of 2,3,7,8-TCDD in paired serum and adipose tissue samples collected from the same individuals. The analysis of each blood sample for total and free cholesterol, triglycerides, HDL, and phospholipids will allow us to examine the distribution of 2,3,7,8-TCDD in the various lipid compartments of blood.

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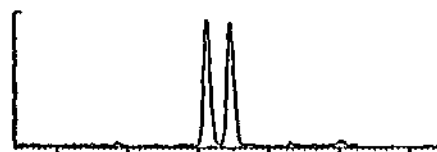
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MASS	RETENTION TIME	HEIGHT	AREA
319.90	0 HRS 23 MINS 58 SECS	25.9438	188.8838



321.89	0 HRS 23 MINS 57 SECS	32.4174	217.9545
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331.94	0 HRS 23 MINS 58 SECS	583.6873	3873.7650
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333.93	0 HRS 23 MINS 58 SECS	848.0822	6352.4980
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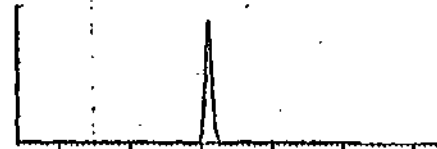


Figure 1. Mass chromatograms from a 10-g sample of pool L (1.6 ppt) showing separation between 2,3,7,8- and 1,2,3,4-TCDD.

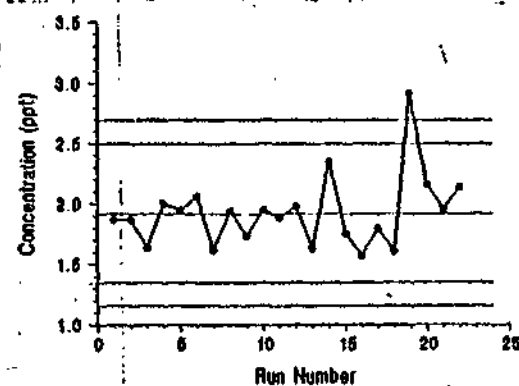


Figure 2. Quality control chart for spiked human serum pool L (10-g samples).

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Use of trade names is for identification only and does not constitute endorsement by the Public Health Service or the U.S. Department of Health and Human Services.

Table I. Estimated Concentration (Parts per Trillion in a 10-g Sample) and Linear Regression Parameter Estimates from Mass Spectrometry Calibration

95% control limits		calibrator concn	obsd mean concn	bias, %	std dev	coeff of variation, %
lower	upper					
0.0139	0.0346	0.025	0.0243	-3	0.0053	22
0.0384	0.0595	0.050	0.0490	-2	0.0053	11
0.0793	0.1012	0.100	0.0900	-10	0.0054	6
0.2438	0.2935	0.250	0.2687	7	0.0127	6
0.4676	0.5148	0.500	0.4912	-2	0.0121	2
Intercept		slope		coeff of determinations		
0.000816705		0.0241131		0.9941		

INITIAL TABLE WIDTH IS DOUBLE COLUMN

Table II. Statistical Data for the Human Serum QC Pools

	H, ppt ^a	I, ppq ^b	L, ppt ^a
concn of 2,3,7,8-TCDD	6.83	25.8	1.93
N (sample size, g)	8 (10)	20 (200)	22 (10)
std dev (σ)	0.64	3.4	0.30
coeff of variation	9.4	13.0	15.5
99% control limits, upper	8.48	34.4	2.70
99% control limits, lower	5.18	17.1	1.16
95% control limits, upper	8.08	32.3	2.51
95% control limits, lower	5.57	19.2	1.35
m/z 320/322 ratio	86.7	79.3	80.4
N (sample size, g)	8 (10)	20 (200)	22 (10)
std dev (σ)	2.6	9.45	6.28
coeff of variation	2.9	11.9	7.8
99% control limits, upper	93.3	103.7	96.6
99% control limits, lower	80.1	64.9	64.2
95% control limits, upper	91.7	97.9	92.7
95% control limits, lower	81.7	60.8	68.1
m/z 332/334 ratio	77.6	77.1	75.0
N (sample size, g)	8 (10)	20 (200)	22 (10)
std dev (σ)	6.2	5.12	4.04
coeff of variation	8.0	6.6	5.4
99% control limits, upper	93.7	90.3	85.4
99% control limits, lower	61.6	63.9	64.6
95% control limits, upper	89.8	87.1	82.9
95% control limits, lower	65.4	67.0	67.1

^aThese pools spiked with dioxins and furans described in text.

^bThis pool unspiked composite serum from 67 individuals.

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Table III. Validation of CDC Quantitation Stock Solution Against EPA and NBS Material for 2,3,7,8-TCDD

	reported concn ^a	found ^b using CDC standard curve				N	% bias
		mean ^c	std dev	coeff of variation			
NBS ^c SRM 1614	1746-01-6 67.8 ± 2.3	69.4	3.0	4.3	4	+2.4	
EPA, ^d 7.87 ± 0.78 µg/mL, CAS: 17496-01-6	78.7 ± 7.9	79.6	2.7	3.4	4	+1.1	
CDC-A ^e	3.77	3.34	0.22	6.8	4	-11	
CDC-B ^e	5.02	4.46	0.23	6.2	4	-11	
CDC-C ^e	25.1	24.9	1.51	6.1	4	-0.8	
CDC-D ^e	50.2	49.4	4.23	8.6	4	-1.6	
CDC-E ^e	125.6	123.4	7.47	6.1	2	-1.7	

^aConcentration in pg/µL. ^bEach standard was made in duplicate and each vial was analyzed on two different days. 2400-pg of [¹³C₁₂]-2,3,7,8-TCDD was added to each vial as internal standard. After evaporation to dryness, the vials were reconstituted to 50 µL with toluene prior to mass spectral analysis of 2 µL aliquots. ^cA 25-µL aliquot of this standard was added to each vial. ^dThese standards were diluted 1:100 before 2-µL aliquots were taken. ^eThese standards were prepared by an additional 1:10 dilution of the stock solution used to make CDC-C, D, and E. The increased bias for these two standards may reflect the extra 1:10 dilution of the stock solution required to prepare these two standards.

INITIAL TABLE WIDTH IS DOUBLE COLUMN

Table IV. Recoveries of Internal Standard and Native 2,3,7,8-TCDD "Spiked" Human Serum

aliquot added	target ^a	found (200-g samples)					
		1	2	3	4	mean obsd	bias, %
A	49.8 ± 5.1	42.0	39.0	32.0	64.2	44.3 ± 12.0	-11.0
B	72.2 ± 3.5	78.5 ^b	65.5	74.0	80.9	74.7 ± 5.9	+3.5
C	95.5 ± 6.9	75.5	73.5	90.0	112.5	87.9 ± 15.6	-8.0

[¹³C₁₂]-2,3,7,8-TCDD (% recovery)

200-g samples of human serum spiked with 240 pg of [¹³C₁₂]-TCDD

56, 50, 84, 93, 48, 63, 81, 80, 66, 59, 76

50-g samples of human serum spiked with 240 pg of [¹³C₁₂]-TCDD

58, 58, 63, 51, 64, 32

10-g samples of human serum spiked with 240 pg of [¹³C₁₂]-TCDD

85, 68, 61, 54, 50, 100, 77

^aThe target value was calculated by adding calibrated aliquots to the pool I ($x = 25.8 \pm 3.4$ ppq). Aliquot A = 24.0 ± 3.8 ppq ($N = 5$); B = 46.4 ± 0.6 ppq ($N = 3$); C = 69.7 ± 6.0 ppq ($N = 5$). ^bUndetermined amount of sample spilled. The internal standard ion counts were low.

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Table V. Within-Vial Variability

sample	day 1 pg (pptr)	day 1 pg (pptr)	maximum % bias	average % bias
1	19.7 (1.87)	18.9 (1.79)	4.2	5.4
2	19.8 (1.87)	21.0 (1.98)	6.1	
3	14.7 (73.5) ^a	13.5 (67.5) ^a	8.9	
4	4.3 (21.5) ^a	4.4 (22.0) ^a	2.3	
	day 1 pg (pptr)	day 2 pg (pptr)	maximum % bias	average % bias
5	60.7 (5.77)	69.7 (6.62)	14.7	5.7
6	57.3 (5.49)	56.4 (5.40)	1.6	
7	71.9 (3.45)	75.6 (3.62)	5.1	
8	48.0 (1.53)	47.5 (1.51)	1.1	
9	78.0 (1.85)	82.5 (1.96)	5.8	
	day 1 pg (pptr)	day 5 to 18 pg (pptr)	maximum % bias	average % bias
10	12.8 (64.2) ^a	11.7 (58.7) ^a	9.4	7.9
11	6.6 (33.4) ^a	6.4 (32.4) ^a	3.0	
12	5.2 (26.2) ^a	5.1 (25.7) ^a	1.9	
13	5.4 (27.0) ^a	4.6 (23.2) ^a	16.4	
14	39.6 (182) ^a	40.4 (185) ^a	2.0	
15	36.4 (5190) ^a	41.8 (5960) ^a	14.8	
	day 1 pg (pptr)	day 27 pg (pptr)	maximum % bias	average % bias
16	18.6 (1.75)	18.7 (1.76)	0.6	9.9
17	18.6 (1.77)	13.7 (1.30)	36	
18	38.9 (1.85)	41.8 (1.98)	7.0	
19	53.9 (1.71)	51.5 (1.64)	4.3	
20	75.3 (1.79)	76.7 (1.82)	1.7	

^aParts-per-quadrillion.

INITIAL TABLE WIDTH IS SINGLE COLUMN

Table VI. Quantitation of Combined Aliquots of QC Pool L

expt	level, g	expected* X ± std dev pg (ppt)	obsd pg (ppt)	% bias
1	10.6	20.5 (1.93 ± 0.29)	18.6 (1.76)	-9.1
	10.53	20.3 (1.93 ± 0.29)	18.6 (1.77)	-8.5
	21.06	40.6 (1.93)	38.9 (1.85)	-4.3
	31.45	60.7 (1.93)	53.9 (1.71)	-11.2
	42.14	81.3 (1.93)	75.3 (1.79)	-7.4
2	21.115	40.8 (1.93)	44.4 (2.1)	+8.9
	31.795	61.4 (1.93)	59.5 (1.87)	-3.0
	42.369	81.8 (1.93)	105.2 (2.48)	+28.6
3	10.525	20.3 (1.93 ± 0.29)	21.1 (2.0)	+3.9
	20.984	40.5 (1.93)	39.1 (1.86)	-3.4
	31.587	61.0 (1.93)	69.1 (2.19)	+13.3
	42.152	81.4 (1.93)	88.5 (2.1)	+8.8

*See Table II for QC pool L data.

INITIAL TABLE WIDTH IS SINGLE COLUMN

Table VII. Concentration of 2,3,7,8-TCDD in Human Plasma, Whole Blood, and Serum Samples

pooled serum, no. of persons	sex	race	age	concentration	
				whole weight ^a	lipid weight ^b
10				42.0	c
11				29.0	c
8				9.5	c
3				21.0	c
9				12.2	c
4				22.2	c
67				25.8	4.2
78				29.5	c
107				19.8	c
d				19.6	c
d				31.9	c
d				10.9	c
d				12.8	c
e	M	W	28	14.0	c
e	F	W	59	54.5	c
e	M	W	27	48.0	c
e	F	W	30	51.0	c
e	M	B	51	26.5	c
f	M	W	58.2	37.6	c
f	M	W	26.8	53.5	10.2
f	F	B	18.9	18.8	2.77
f	M	W	49.9	63.0	8.7
f	M	W	23.9	13.5	1.87
f	F	B	40.9	34.6	4.88
f	M	W	23.1	21.7	3.04
f	F	B	33.6	39.1	5.74
f	F	W	58.6	45.4	7.08
f	M	W	58.0	83.1	12.0
f	M	W	59.5	28.8	4.91
f	M	W	35.4	24.2	3.07
f	M	W	70.0	211	26.0
f	F	W	37.0	142	21.9
f	F	W	48.6	30.0	4.10
f	F	W	43.2	17.2	4.93
f	F	W	63.6	58.8	9.43
f	F	W	37.4	45.8	11.94
f	M	W	45.2	22.0	4.44
f	F	W	48.1	24.1	4.22
f	F	W	40.5	24.5	4.72
f	F	W	31.3	15.0	2.88

^aConcentration in ppq. ^bConcentration in ppt. ^cPercent lipid not determined. ^dPlasma sample from 4 different individuals. ^eWhole blood sample (lysed cells) from 5 different individuals. ^fSerum sample from 22 different individuals.

INITIAL TABLE WIDTH IS DOUBLE COLUMN

Table VIII. Concentration of 2,3,7,8-TCDD in Human Serum and Adipose Tissue from Individuals with No Known TCDD Exposure

	<i>N</i>	mean, ppt	range, ppt
present study: human serum on lipid-weight basis	21	7.6	1.9-26.0
human adipose, Patterson et al. (14)	57	7.4	1.4-20.2
human adipose, Patterson et al. (15)	35	7.1*	2.7-19
human adipose, Graham et al. (31)	36	7.2*	
human adipose	61 ^b	7.5	1-16
human adipose, Schecter et al. (12)	25	6.4	ND, ^c 2.0-13
	8	7.2	1.4-17.7

*Geometric mean. ^bCombination of results from 13, 32, and 33. Three results from persons known to have had exposure to 2,4,5-trichlorophenol were excluded. *ND, not detected. ^c

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