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**Description Notes** Alvin L. Young filed this item under "Vietnam Veterans Twin Study." Item includes: one report of contact dated May 3, 1984, discussing Gene Hufford's call to Seth Eisen inviting Eisen to present an overview of the Vietnam Experience Twin Study to the Senate Veterans Affairs Committee; one report of contact dated May 4, 1984, discussing Seth Eisen's call to Larry Hobson regarding the briefing to the Senate Veterans Affairs Committee; one routing slip from Seth Eisen to Dr. Alvin Young; and one copy of a Letter to the Editor about Twins in the July 5, 1984 issue of the New England Journal of Medicine, page 58.



### REFERENCE SLIP

TO (Name or title—Mail routing symbol)	INITIALS—DATE
1. DR ALVIN YOUNG	
2.	
3.	
4.	
5.	


REASON FOR REFERENCE

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REMARKS

The attached might be of interest.  
Any advice?

FROM



DATE

5/4/

FEL/EXT.

REPORT OF CONTACT

Contacted By: Gene Hufford, Legislative Affairs (101E), VACO,  
389-5004

Date of Contact: 5/3/84

Hufford called to invite me to present an overview of the VETS to the Senate Veterans Affairs Committee in Washington on Wednesday, May 16 in the Senate Veteran Affairs Hearing Room, Room 412.

The briefing will be to the committee's majority staff, will be informal, and will take about 1 1/2 hours. I will be expected to give an initial presentation which, he suggested, might include:

history and background of the VETS

purpose

"parameters" (scope)

a discussion of which portions of the project are being contracted and which are the responsibility of VA employees

estimated cost

Hufford suggested that I particularly be prepared to answer questions relating to possible duplications between the VETS and the Vietnam Veteran Needs Survey.

The VA attendees have not yet been identified, although probably Boren and Hufford will both accompany me.

Seth Eisen

cc: Medical Center Director  
COS  
ACOS R&D

## REPORT OF CONTACT

Contacted: Larry Hobson  
Date of Contact: May 4, 1984

I called Larry for advice about my upcoming briefing to the Senate Veterans Affairs Committee.

Larry said that the request for the briefing was initiated by the Senate. (Sometimes the VA requests permission to give a briefing.) Larry does not know what stimulated the request, although it may have been in response to the VA's request that the Senate committee ask OTA to review our proposal.

Gronvol asked Boren to select the VA staff person to respond. Greene was initially asked. However, Hobson approached someone in Gronvol's office and strongly suggested that an alternative to Greene be identified "except if your intention is to kill the study." Hobson said it was easy to persuade the VA to send me instead of Greene. However, Greene will probably be present at the briefing, along with Boren and several others (not yet selected).

Larry said that although I will be presenting to the Senate committee, House Veterans Affairs Committee members may also be present, since there is interest in our proposal on both sides of Congress. Larry said in my presentation, I should assume that staff members have no technical knowledge, that they are "green". "They may be bright but have little background."

Larry said that the briefing will be informal (participants sitting at a table) and will most likely be cordial and polite. However, John Steinberg, the senior minority staff member, can sometimes be difficult. Steinberg "enjoys making people uncomfortable." He tends to ask questions "as if he is a prosecuting attorney." The questions are typically intended to indicate "how much he knows" and frequently imply an answer by the manner in which they are asked. He is usually well prepared. Questions should be answered politely and directly. Don't permit Steinberg to conclude something which isn't true. While some senators and staff don't like Steinberg, he is apparently one of Cranston's favorites.

Hobson suggested my presentation should be limited to 30 minutes and preferably only 20. He felt that slides are usually awkward but the distribution of a simple paper document which outlines my important points might be appropriate. At least one item which should be included in my briefing is a statement that the VETS does not replicate any completed, planned, or ongoing study.

Hobson suggested that the committee might be particularly interested in answers to the following questions:

1. How does the VETS differ from other studies (particularly the Veterans Needs Assessment study)? The response

circulating at VACO is that the Needs Assessment study is hypothesis seeking and therefore will use different instruments than the VETS will.

2. Why should Congress support a study like the VETS for which Agent Orange assessment is only a relatively minor portion? VACO's response has been that there is only one true AO study - Ranch Hand. AO exposure cannot be accurately determined for any other research project. However, veterans believe something in Vietnam damaged their health. The answers provided by the VETS will help respond to this broader question.

3. Why not wait until the CDC and Needs Assessment studies are completed before initiating the VETS? VACO's answer has been that veterans are appropriately clamoring for studies and answers now. To base the VETS on data obtained from research presently in progress will result in unacceptable delays.

4. Why should the VETS be performed by the VA rather than some other group (such as CDC)? VACO's answer: VETS is a well conceived and detailed study. Therefore, like the Ranch Hand, it can be competently performed without fear of charges of bias. If such charges do surface, the VA can provide the raw data for review by any other group.

4. What is the VETS budget?

5. What is the VETS timetable? Hobson suggested that I be polite but vague in answering this question.

I asked Larry about the appropriateness of discussing with the committee some of the problems facing the VETS, for example: the difficulties dealing with OMB during their ongoing review of our questionnaires and obtaining release of certain information from the Social Security Administration. Hobson said that I should address this question to someone in Gronvol's office. I also asked about bringing the revised protocol to the briefing. Initially, Larry seemed to think this was an excellent idea, since it would graphically demonstrate the high quality effort which has been invested in the project. However, he later suggested that if given the opportunity to review our protocol, staff members may attempt to play scientist and ask for written responses to literally tens of questions they will later send us.

Larry and I briefly discussed the possibility that Greene may openly disagree with some of my statements before the Senate committee. Hobson felt this was unlikely but possible and that there is no easy way to deal with this threat.

## ERROR IN PRENATAL DIAGNOSIS BY DNA ANALYSIS

*To the Editor:* In May 1983 we presented our five years' experience with DNA analysis for prenatal diagnosis of hemoglobinopathies.<sup>1</sup> At that time we reported on 95 cases, 78 of which had been subsequently studied. In all these 78 cases the prenatal diagnosis was proved to be correct. Since that time the applicability of prenatal testing for sickle-cell anemia by DNA studies has been improved because of the development of a direct detection analysis using the endonuclease *MstII*<sup>2,3</sup> or its isoschizomer, *CvuI*. Our total experience is now with just over 300 pregnancies studied for a hemoglobinopathy risk. Follow-up studies have now been carried out in 145 of these cases, and a single mistake has been discovered (error rate, 0.7 per cent). In this instance *MstII* analysis of DNA from a fetus at risk for sickle-cell anemia led to a diagnosis of an unaffected fetus with sickle-cell trait. The product of this pregnancy was an infant with sickle-cell anemia.

This mistake was in all likelihood caused by very-low-level contamination of the fetal DNA sample with exogenous plasmid DNA. This contaminating plasmid contained the 1.8-kb *BamHI* human fragment that was used as a probe in the hybridization phase of the Southern blot analysis. Because the plasmid was originally constructed from a normal  $\beta$ -globin gene that lacked the sickle-cell mutation, *MstII* digestion of the plasmid yielded a fragment identical in size to the normal  $\beta$ -globin allele. The final autoradiogram displayed the pattern of a person with sickle-cell trait, but the  $\beta^S$  fragment was entirely fetal in origin, and the  $\beta^A$  fragment was non-fetal (i.e., plasmid) in origin. It is calculated that approximately  $10^{-5}$   $\mu$ g of plasmid DNA would produce, after hybridization, the intensity of signal equivalent to that seen in 5  $\mu$ g of genomic DNA. This contamination occurred despite the fact that we use separate glassware, solutions, and automatic pipettors for genomic DNA as opposed to nongenomic (plasmid) DNA. We believe this type of error has also been seen in other laboratories.

The frequency of this type of error in Southern blotting experiments may be greatly reduced by the use of carefully selected probes. Depending on the genomic fragments being examined, cDNA probes, single-stranded probes, or probes one of whose end points lies within the genomic fragment being examined may be useful in avoiding this type of error. If contamination of patient DNA with probe DNA occurs, the size of the hybridizing fragment of probe origin will be different from any of the expected genomic fragment sizes and, therefore, will not interfere with the interpretation of the results. We are in the process of constructing a new probe of this type, which should be available to interested laboratories by the time this letter appears.

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- Orkin SH, Little PFR, Kazazian HH Jr, Boehm CD. Improved detection of the sickle mutation by DNA analysis: application to prenatal care. *N Engl J Med* 1982; 307:32-6.
- Chang JC, Kan YW. A sensitive new prenatal test for sickle-cell anemia. *N Engl J Med* 1982; 307:30-2.

## TWINS

*To the Editor:* Hrubec and Robinette (Feb. 16 issue)<sup>1</sup> note that in an aggregate of twin pairs, the proportions that are monozygotic and dizygotic can be estimated using Weinberg's rule. However, they do not comment on the accuracy of the rule. Its basis is the assumption that among dizygotic pairs, the numbers of same-sex and opposite-sex pairs are almost exactly equal.

A review<sup>2</sup> of studies of a total of 1334 dizygotic twin pairs identified and blood-typed at birth suggests that same-sex pairs outnumber opposite-sex pairs in a ratio of about 8:7. The difference between the observed ratio and that of 1:1 postulated by Weinberg is significant ( $P < 0.01$ ). Taking the estimate of 8:7 as correct, the

number of dizygotic twins in an aggregate may be estimated as  $(15/7)U$  (rather than  $2U$ ), where  $U$  is the number of opposite-sex pairs.

It is interesting to see to what extent the use of Weinberg's rule produces biased estimates of the proportions of monozygotic and dizygotic pairs in a sample. Contrary to the assertion of Hrubec and Robinette, the total twinning rate in the United States and Europe<sup>3</sup> is no longer around 12 per 1000 but has declined to less than 10 per 1000. Table 1 gives typical values of monozygotic and dizygotic

Table 1. Typical Values of Monozygotic (MZ) and Dizygotic (DZ) Twinning Rates as Estimated by Weinberg's Rule and by the Suggested Reformulation.

	ESTIMATED DZ RATES		ESTIMATED MZ RATES		TOTAL
	WEINBERG	REFORMULATION	WEINBERG	REFORMULATION	
Europe and U.S.	6.5	7.0	3.5	3.0	10.0
Nigeria <sup>4</sup>	34.5	37.0	5.5	3.0	40.0

twinning rates as estimated by Weinberg's rule and by the above reformulation of it.

It is evident that (1) where dizygotic twinning rates are moderate (as in white populations), the Weinberg estimate of monozygotic rates may be acceptable, if slightly high, and (2) where dizygotic rates are high (as in Nigeria), the Weinberg estimate of monozygotic rates may be almost double the true rates.

It may be shown that if there were no true variation in monozygotic rates, then the use of Weinberg's rule would suggest that monozygotic rates "mimic" dizygotic rates. One may wonder whether the (admittedly slight) variations in monozygotic rates (based on Weinberg estimates) with race and maternal age are merely a spurious consequence of a flaw in Weinberg's rule.

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- Hrubec Z, Robinette CD. The study of human twins in medical research. *N Engl J Med* 1984; 310:435-41.
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## VIDEO-GAME PALSY: DISTAL ULNAR NEUROPATHY IN A VIDEO-GAME ENTHUSIAST

*To the Editor:* An occupational paralysis of the muscles supplied by the deep palmar branch of the ulnar nerve was first described in 1896 under the title "A Peculiar Form of Progressive Muscular Atrophy in Gold Polishers."<sup>1</sup> The neuropathic origin was recognized by Hunt in 1908 when he reported distal ulnar neuropathy after prolonged oyster opening.<sup>2</sup> Cases have also followed shoveling with a spade,<sup>1,3</sup> carpentry, and use of vibrating buffers, wire cutters, leather-cutting knives, floor polishers, and pneumatic drills. Other causes include laceration, carpal-bone or radius fracture, scar-tissue contracture, ulnar-artery disease, anomalous muscles, osteoarthritis, ulnar-nerve tumor, lipoma, and hemorrhage.<sup>1,3,4</sup> Distal paralysis of the ulnar nerve at the wrist has also been described in motorcyclists and bicyclists.<sup>1,5</sup> We now report distal ulnar neuropathy in a video-game player.

A 28-year-old man noted loss of feeling in the medial two fingers of the left hand for two months, with weakness of the left hand and callus formation on the base of the left hypothenar eminence. Clawing of these two fingers was also noted, with difficulty in spreading the fingers apart. For one month he had played video games four to six times a day (10-minute duration of each game). While playing the games, he rested the extended left hand on the machine, with

pressure on the hypothenar eminence (at the site of the callus), and used the left fingers to turn a rotary knob. He stopped playing the games three weeks before being seen, with some improvement of sensory symptoms.

Examination revealed *hypoesthesia to pin and touch* over the fifth finger, the ulnar side of the fourth finger, and the ulnar side of the hand on the left. Mild wasting of the left hypothenar eminence was noted, without fasciculations. There was severe weakness of the first dorsal interosseous and the abductor digiti minimi. He could not cross the left fifth and fourth fingers, and Froment's sign was present on that side. Mild clawing of the left hand was observed, with a callus over the base of the left hypothenar eminence. The remainder of the examination was normal. An electromyogram revealed positive waves and fibrillations of the left first dorsal interosseous and hypothenar muscles, with diminished recruitment. Motor distal latency was prolonged (5.4 msec) after left-ulnar-nerve stimulation. X-ray examination of the wrists was negative.

This recreational neuropathy probably resulted from excessive pressure on the deep branch of the ulnar nerve in the extended hand. As expected from the location of the callus, both the deep and superficial branches were affected (Type I syndrome described by Shea and McClain<sup>4</sup>).

Video games have become a popular form of recreation, but the hazards of this activity have not been well established. Video games may affect subjects with light-sensitive epilepsy,<sup>6</sup> and prolonged playing may cause wrist pain ("space-invaders wrist"<sup>7</sup>) or de Quervain's stenosing tenosynovitis.<sup>8</sup> The present case documents a new complication.

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JAMES N. ST. JOHN, M.D.

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#### UNNECESSARY PSYCHIATRIC HOSPITALIZATION

*To the Editor:* Dr. Mosher asks why studies showing the efficacy of alternatives to psychiatric hospitalization have failed to result in widespread use of such alternatives, and offers some reasons (Dec. 22 issue).<sup>\*</sup> Some reasons that he does not discuss are also important.

A psychiatrist faced with an ill patient will make the decision about hospital admission with reference to the individual case, not to a summary of research studies. Most of us know there is small statistical likelihood that even a potentially suicidal patient will actually kill himself or herself within the next three or four weeks, no matter what we do, but few of us will take even a small risk with the life of a patient under our care. A number of studies have demonstrated the efficacy of drugs and electroconvulsive therapy in the treatment of severe depressions. These treatments are more easily given in the supervised environment of the hospital. Moreover, a doctor's legal liability is smaller if the patient commits suicide after all due safeguards have been applied (hospitalization, "suicide precautions") than if the patient does it at home after the doctor has

decided against hospitalization. For such reasons psychiatrists will continue to put very ill people in hospitals, as long as hospitals are available.

Abuse of hospitalization occurs in another group: people who are not very ill but are admitted because it is economically more convenient. Dr. Mosher has mentioned the unfortunate bias against outpatient care in many health-insurance policies. General hospitals in many areas have "overbuilt" psychiatric units, including beds in alcoholism and chemical-dependency treatment centers. Such hospitals have a vested interest in keeping those beds full, and some administrators become distressed when alternatives to hospitalization make a dent in the census.

There is also the well-known but little-discussed probability that many psychiatrists make more money per hour from hospital patients than from office patients. In the office we customarily charge for our time. In the hospital we customarily charge by the visit or by the week, as do other specialists. Psychiatrists who hospitalize many of their patients often spend less time for the dollar on inpatients than on outpatients. It is too easy to find a reason for admitting a patient or prolonging his or her hospital stay when it is to our economic advantage to do so, however incorruptible we may think we are.

The enormous cost of hospital care and data on the effectiveness of outpatient treatment can result in more appropriate and conservative use of hospitalization, but this will not happen until the economic advantage of outpatient treatment becomes comparable to that of inpatient treatment, until peer review has real teeth in it, and until hospitals can figure out what to do with all the empty space that will result.

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*To the Editor:* I wholeheartedly agree with Dr. Mosher's persuasive and concise analysis. However, I would like to extend the list of presumed obstacles in translating research evidence into practice by adding one point, which I consider important. A shift from inpatient to ambulatory psychiatric care suggests changes in prevalent treatment methods and in the type of person providing them. Drug treatment is necessary and effective in both inpatient and outpatient settings and remains the exclusive domain of psychiatrists, whereas nonpharmacologic approaches — in particular, behavioral therapies, crisis intervention, and couple and family therapy — are methods frequently employed in ambulatory care and are mostly provided by nonmedical mental-health professionals (i.e., clinical psychologists, social workers, and psychiatric nurses). Since traditional training in psychiatry places less emphasis on these methods than it does on pharmacologic and individual psychotherapy, a shift from hospital to ambulatory care also suggests an increasing shift in responsibilities from psychiatrists to nonmedical professionals. Whereas the latter would certainly welcome this expansion of responsibilities, it represents a threat to the traditional image and practice of psychiatry, and it would necessitate dramatic changes in psychiatric-residence curricula, as well as some retraining of current practitioners. Last but not least, the reduced cost of ambulatory care can be partially attributed to the lower cost of employing more nonmedical therapists.

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The above letters were referred to Dr. Mosher, who offers the following reply:

*To the Editor:* Both these letters amplify my article in important ways. Dr. Hudgens is courageous in detailing the abuses of hospitalization, and some reasons for them, that occur in the practice of psychiatry today. Dr. Linden raises extraordinarily important issues of professional territoriality and training. Except for a small number of programs, current psychiatric training does little to equip medical doctors to deal with the psychosocial issues relevant to the care of severely disturbed and disturbing persons living in the com-

<sup>\*</sup>Mosher LR. Alternatives to psychiatric hospitalization: why has research failed to be translated into practice? *N Engl J Med* 1983; 309:1579-80.