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.
The attached might be of interest.  

Any advice?
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 indicated "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 on 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.

5. What is the VETS budget? 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 PREGNAT DIAGNOSIS BY DNA ANALYSIS

To the Editor: In May 1983 we presented our five years' experience with DNA analysis for prenatal diagnosis of hemoglobinopathies. 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 Msii that digests the DNA into monomeric structural DNA. 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 Msii 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, Msii digestion of the plasmid yielded a fragment identical in size to the normal beta-globin alpha fragment. The final autoradiogram displayed the pattern of a person with sickle-cell trait, but the b alpha fragment was nonfetal (i.e., plasmid) in origin. It is calculated that approximately 10^-3 μg of plasmid DNA would produce, after hybridization, the intensity of signal equivalent to that seen in 5 μg 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 used 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.

CORNIE D. BOHM, M.S.
HAID H. KAZAZIAN, JR., M.D.
Johns Hopkins University
School of Medicine

Baltimore, MD 21205


TWINS

To the Editor: Hrubec and Robinette (Feb. 16 issue) 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- and opposite-sex pairs are almost exactly equal.

A review 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 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 twinning rates as estimated by Weinberg's rule and by the suggested reformulation.

<table>
<thead>
<tr>
<th>Country</th>
<th>Estimated DZ Rates</th>
<th>Estimated MZ Rates</th>
<th>Total Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe and U.S.</td>
<td>6.5</td>
<td>7.0</td>
<td>3.5</td>
</tr>
<tr>
<td>Nigeria*</td>
<td>34.5</td>
<td>37.0</td>
<td>3.5</td>
</tr>
</tbody>
</table>

*The total twinning rate in Europe is no longer around 12 per 1000 but has declined to less than 10 per 1000. The values given are typical.

TABLE 1. TYPICAL VALUES OF MONOZYGOTIC (MZ) AND DIZYGOTIC (DZ) TWINS AS ESTIMATED BY WEINBERG'S RULE AND BY THE SUGGESTED REFORMULATION.

WILLIAM H. JAMES, PH.D.
Medical Research Council
London NW1 2HE, England
Mammalian Development Unit


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." The neuropathic origin was recognized by Hunt in 1908 when he reported distal ulnar neuropathy after prolonged oyster opening. Cases have also followed shoveling with a spade, 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. Distal paralysis of the ulnar nerve at the wrist has also been described in motorcyclists. We now report distal ulnar neuropathy in a video-game player.

A 26-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 game three weeks before being seen, with some improvement of sensory symptoms.

Examination revealed hypaesthesia 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 Frenen's sign was present on the ulnar side of the left hand. 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 (5.3 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 Shek and McClain). 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, and prolonged playing of "space-invaders" ("space invaders wrist") or de Quervain's tenosynovitis. The present case documents a new complication.

ROBERT P. FRIEDLAND, M.D.
JAMES N. ST. JOHN, M.D.
Martinez, CA 94553 Veterans Administration Medical Center

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). 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 evidence to support 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 and 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, unless peer review has real teeth in it, and until hospitals can figure out what to do with all the empty space that will result.

RICHARD W. HUDGENS, M.D.
St. Louis, MO 63141 777 S. New Ballas Rd.