

AIDS Blood Test: Qualified Success

The AIDS blood-screening test got its first-semester grades at a meeting of AIDS researchers and industry representatives last week in Bethesda, Md. The consensus: The test earns an A for cleaning up the blood supply. But it gets lower marks for its specificity, because it falsely identifies some people as "positive" for antibodies to the virus. The meeting was sponsored by the Food and Drug Administration (FDA), the National Institutes of Health (NIH) and the Centers for Disease Control (CDC).

Meeting participants compared notes on data collected since the first AIDS blood screen was approved on March 2, nine months after the virus was made available to manufacturers (SN: 3/9/85, p. 148). While there were minor discrepancies within the overwhelming amount of data presented, the test testers say the blood screen is nearly 100 percent accurate in identifying all blood samples that contain antibodies to the virus associated with AIDS.

As of Aug. 5, according to the CDC, 207 transfusion recipients and 83 hemophiliacs have gotten AIDS from blood or blood products. But while removing AIDS-tainted blood will stop *new* blood-related transmission, the incidence of blood-associated AIDS is expected to tail off slowly, since AIDS can appear more than five years after receipt of contaminated blood (SN: 5/25/85, p. 328).

In general, conference participants were optimistic about the test and pessimistic about the syndrome. "The infection has a big jump on us," says James W. Curran, head of CDC's AIDS task force. Only 2 percent of the 12,107 documented adult AIDS cases (about half of whom have died so far) were the result of receiving blood or blood products. "I think we have solved the problem of transfusion; we have much to do with the other 98 percent of cases," says Curran.

Three representatives of test manufacturers reported at the meeting that the test's sensitivity rate — its ability to identify people with the viral antibodies — is in the 99 percent-plus range. But the test falters in the area of specificity. Of more than 1 million blood unit reports tabulated by the FDA, 0.85 percent were initially positive but only 0.25 percent were positive on repeat testing. And in an American Red Cross/CDC analysis of 2,552 repeatedly reactive specimens, only 23 percent of those were positive by a more exact but more difficult confirmatory test.

In the current test, called ELISA for enzyme-linked immunosorbent assay, blood serum is placed in wells containing pieces of the AIDS virus. If antibodies to the virus are present in the blood, they will

stick to viral fragments and can be detected by an added chemical that causes a color change. The confirmatory "Western blot" test is more exact — it detects not only antibody presence but also antibody size. Proteins from the virus are spread on a special paper. Blood serum is added, and if antibodies are present they can be detected and sized; only those that are the same size as known antibodies to AIDS are accepted as a positive result.

The ELISA, many of the researchers pointed out at the meeting, was designed as a quick, inexpensive and accurate way to safeguard the blood supply, not as a screen for people with AIDS. The specificity weakness is relatively minor as long as the test is used for its intended purpose, they note.

The high false positive rate means some antibody-free blood will be discarded, but not to the point where it will critically affect blood bank supplies, say the researchers. But it does present the dilemma of what to tell a person with positive results, since not all positive ELISA tests represent antibodies to the AIDS virus, and since the prognosis for people with antibodies — even if confirmed by Western blot — remains to be determined.

The false positive rate is disproportionately high in women, who represent only about 7 percent of AIDS cases

but nearly half the repeatedly positive ELISA tests. One possible reason discussed at the meeting was initially suggested in the May 25 LANCET by University of Frankfurt researchers. At the time of delivery, some mothers develop antibodies against proteins on the surface of foreign (i.e., the baby's) white blood cells. In the ELISA test, these antibodies could, in turn, recognize and react with protein that the AIDS virus has picked up from the host white blood cell in which it was grown. The result would be a positive test, though no antibodies specific to the AIDS virus would be present.

Several companies are working on a second-generation test that uses recombinant-DNA-produced proteins instead of viral fragments as an antibody target in the ELISA assay. A researcher from one such company, Centocor in Malvern, Pa., noted that the recombinant DNA system promises a constant and plentiful supply of virus-related protein without the hazards of working with the virus. In addition, using recombinant DNA eliminates false positives that arise from cross reactions with extraneous cell debris included in the virus portion. Farther down the line are viral testing kits.

In summing up the performance of a test that entered the market incredibly quickly — only nine months after manufacturers had the virus to work with — Joseph Bove of the Arlington, Va.-based American Association of Blood Banks says, "We have a lot to learn, but if in any way the past is prologue, I'm encouraged that we will learn it quickly." —*J. Silberner*

Supernova encounter of a third kind

Supernovas are usually discovered by accident: Astronomers looking at a particular galaxy notice a bright object that was not there before. So it happened to Alexei V. Filippenko of the University of California at Berkeley and Wallace L. W. Sargent of Caltech in Pasadena. They were making a spectroscopic survey of nearby galaxies. On Feb. 28, as they observed galaxy NGC4618, their spectroscope recorded a bright object near the center of that galaxy. The object, now catalogued as SN1985f, has aroused a great deal of interest within the astronomical community. With properties quite different from those of either of the two classes of supernova that astronomers have heretofore known, it is being called the first of a third class of supernova. Moreover, its existence could answer some long-standing questions about mysterious objects called supernova remnants.

Supernovas are intense explosions of stars. The explosion causes such an increase in brightness that the supernova is conspicuous on photos of even fairly distant galaxies. (A supernova in our own galaxy would probably be obvious to everybody without need for telescopes,

but we haven't seen one of those in more than 300 years.) These explosions are characteristic of the last stages of a star's life cycle.

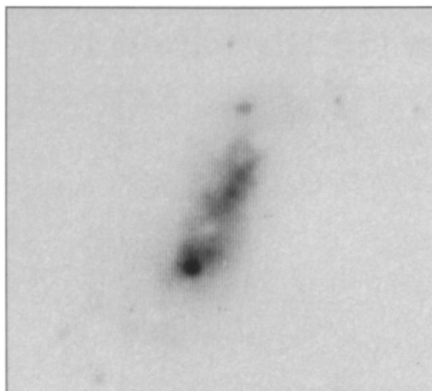
Astronomers believe that type I supernovas occur when a dying white dwarf star with a mass about that of the sun is overwhelmed by matter falling on it from a nearby companion star. The influx causes the white dwarf to explode. Type II supernovas are attributed to the death throes of much larger stars (more than eight times the sun's mass). In old age such a star transmutes lighter elements to heavier ones. It develops a core of iron surrounded by layers of elements lighter than iron ranging to the lightest, helium and hydrogen, at the outermost. As the star makes more and more heavy elements, the core gets overburdened and implodes, sending out a shock wave that explodes the rest of the star.

Type I and type II supernovas are distinguished from each other by differences in maximum brightness, by their light curves (the way their brightness varies over time) and by their spectra. Type III — if SN1985f may be called that — differs from both in all these characteristics, prompting Filip-

penko and Sargent to call it "peculiar" in the title of their paper on SN1985f, published in the Aug. 1 *NATURE*.

Because it was a spectroscope that first found SN1985f, the object's spectrum was the first peculiar characteristic to arrest astronomers' attention. The spectrum is dominated by emission lines, bright resonant emissions at wavelengths characteristic of oxygen, sodium and magnesium. The spectra of type II supernovas also show bright emission lines, but the dominant ones are those of hydrogen and helium, the outermost layers of the exploding star. Oxygen, sodium and magnesium should lie deep within the star. SN1985f is also much dimmer than the other two types of supernova. There is evidence that it never achieved the maximum brightness of either type.

Filippenko and Sargent point out that these characteristics seem to match those of a kind of "peeled" supernova posited some time ago by Roger A. Chevalier of the University of Virginia in Charlottesville. He suggested that a star that had somehow lost its outer layers would explode into a



Chevalier

SN1985f is near center of NGC4618 in this negative print.

supernova much fainter than a usual type II. But Chevalier did not say — nor apparently has anyone else — how such a star might lose its outer layers.

Other astronomers have been rushing to observe SN1985f. One of them, Michael De Robertis of the Lick Observatory, at the University of California at Santa Cruz, points out another peculiarity: In spectra

he has taken between March and July, the intensity of the emission lines does not change. Those of known types of supernova do change over such a 90-day period. This "calls into question" the designation of the object as a supernova, he says. But if it is not a supernova, neither De Robertis nor apparently any other astronomer has suggested what else it might be.

If SN1985f is the representative of a new class of supernova, Filippenko and Sargent point out, it can explain certain strange objects that astronomers have classed as supernova remnants: Cassiopeia A, a very famous radio source; the object N132D in the Large Magellanic Cloud; and "the extraordinary object in NGC4449." Supernova remnants are the clouds of ejecta thrown out by the explosion, which continue to emit light and/or radio for centuries and millennia. From the present condition of Cas A, astronomers can calculate that its explosion should have happened in 1665, but there are no contemporary records of a sighting. If it was type III, it may have been too dim for the naked eye. —D. E. Thomsen

Taking food from thought: Fruitful entry to the brain's word index

Early in 1983, researchers at the University of Maryland and Johns Hopkins University in Baltimore saw a stroke patient with a bizarre problem. Many stroke victims suffer wide-ranging memory losses, but this patient was fine save for his inability to remember the names of many fruits and vegetables. As it turned out, his produce problem provided the scientists with important clues to the "thesaurus-like" ordering of words in the brain.

Although the patient is a sample of one, he displays the most specific organization of categories of words in a discrete brain area yet observed, according to investigators John Hart Jr., Rita Sloan Berndt and Alfonso Caramazza.

The patient, whom they dubbed "M.D.," did not fit into their larger study of gross language problems since he had virtually recovered from several strokes that had occurred almost two years earlier. He complained, however, of difficulty remembering certain "food" words. Further tests suggested that his core problem was with the names of fruits and vegetables. M.D. could, for instance, name pictures of an abacus or a sphinx, but he was dumbfounded when shown an orange or a peach.

Over the next year, to better understand M.D.'s unusual problem, the scientists probed his knowledge of word categories. When asked to name a large number of fruits and vegetables — using drawings, photographs or actual pieces of produce — he was correct just under two-thirds of the time. But when shown other items, such as vehicles, household objects, animals, shapes and trees, he

correctly named nearly all of them. When M.D. had to sort pictures from different conceptual classes into appropriate piles, he again had considerable difficulty only with fruits and vegetables. (The other classes were animals, vehicles and food products.) The same pattern emerged when he was asked to generate as many names as possible from a series of categories and to name items based on verbal definitions or on feeling an object without seeing it.

On the other hand, report the scientists in the Aug. 1 *NATURE*, when provided with the names of fruits and vegetables, M.D. pointed "immediately and with certainty" to the corresponding pictures. He categorized correctly all the written names of fruits and vegetables that had mystified him as pictures.

"It is as if the name is the key to knowledge of fruits and vegetables; the patient cannot find the key for himself," writes psychologist John C. Marshall of Radcliffe Infirmary in Oxford, England, in the same issue. "But, given the name key by the examiner, the patient has no problem in unlocking his apparently intact store of information about fruits and vegetables." According to Marshall, this indicates that M.D.'s brain lesion, which involved the frontal lobe of the cortex and the basal ganglia, impaired part of a "thesaurus-like indexing system of names that give access to the knowledge base represented in the brain."

Cautions Berndt, "We only have data on one patient, but this clearly suggests that items in the mental 'encyclopedia' are organized along specific categories

in the same brain area."

Her claim that the estimated 75,000 words that an educated adult commands may be categorically indexed in the brain goes beyond previous findings with brain-damaged individuals. It is known that left-hemisphere damage can, for example, interfere with memory for faces, colors, color names and numbers. British researchers recently identified more fine-grained disturbances in four brain-damaged patients who were markedly better at naming inanimate objects than they were at naming living things and foods.

"Evidence is beginning to accrue for [Berndt's] claim that there is semantic memory composition in the brain for categories such as vegetables and flowers," comments psychologist Myrna Schwartz of the University of Pennsylvania in Philadelphia. More patients need to be examined for similar category-specific deficits, she adds; this is rarely done with stroke victims. Research in the area is further limited, explains Schwartz, who works with Alzheimer's disease patients, because it is not known how common various language and memory problems are among brain-damaged patients and data are scarce on their language capacities prior to brain damage.

Nevertheless, Berndt says that M.D., who has returned to work at a federal agency, has shown investigators that an adult's vocabulary may be segmented into specific categories that can be disrupted "highly selectively" when the brain is injured. —B. Bower