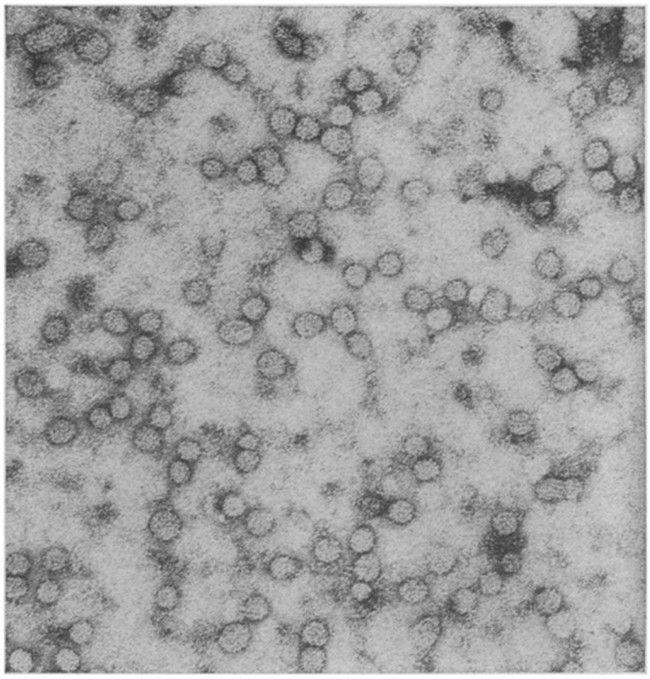
Tests for Australian antigen answer a need

A new antigen can reveal the presence of infectious hepatitis in time to prevent its transmission to blood plasma recipients

by Jeanne Bockel



Abbott Laboratories

An electronmicrograph shows the Australian antigen.

There are two different kinds of viral disease that go by the name hepatitis, or inflammation of the liver. Both cause fever and jaundice. One form, infectious hepatitis, is transmitted through contaminated food and water; the other, serum hepatitis, is the one transmitted through blood transfusions, dirty syringes and hypodermic needles.

Transfused blood causes more than 30,000 cases of hepatitis a year in the United States and of these up to 10 percent die. According to the committee on plasma and plasma substitutes, the incidence of hepatitis is probably even greater than this, but reporting is incomplete.

Serum hepatitis became a critical problem as the use of transfused blood increased in recent years. And though hospitals and blood banks have tried to eliminate carriers as potential donors, there has never been an easy way to identify them. The need for a test, to make the screening thorough, has long been apparent.

Dr. Jacob C. Holper, director of Research and Development of Abbott's Courtland Laboratories, says that screening all blood used in transfusions would reduce the number of transfusion-induced hepatitis cases. Heretofore, usual detection techniques have been elaborate and not suitable for mass screening of donors, and liver function tests take too long for the disease to show up. But new tests, based on fairly routine laboratory antibody-antigen test techniques, now give promise of a widely usable technique.

The recently discovered Australian antigen (AU-HAA), which could be a causative organism for hepatitis (SN: 6/14/69, p. 574), gives screeners something to look for that would indicate hepatitis infection. And the discovery that sheep antibody can be used in the test was important, because human antibody is rare. Hepatitis does not always form detectable antibodies in patients, but is found only in a few cases.

Dr. Baruch S. Blumberg of the Institute for Cancer Research in New York, discoverer of the Australian antigen, described it as a small virus-like particle, composed of proteins, which is present in the blood of many patients with both acute and chronic hepatitis. First discovered in the blood of an Australian aborigine, it was later associated with hepatitis. The antigen is rare in apparently healthy Americans, but in the Far East as much as 10 percent of the population may carry it.

Because the antigen looks like a virus but does not have all the characteristics of one, Dr. Blumberg is investigating the possibility that the AU-HAA is not itself the hepatitis organism but is located and carried along on a virus that can cause hepatitis. The evidence in favor of this theory includes its association with hepatitis, its virus-like appearance, transmission of the antigen and hepatitis by blood transfusion, and the fact that it is present in the nuclei of liver cells of patients with hepatitis, he says.

Whether the Australian antigen is involved or simply associated with serum hepatitis, its presence makes screening of blood donors possible.

In recent months, two methods have been coming to be used to identify blood positive for AU-HAA: the gel diffusion test and the complement fixation test. Both of these are standard laboratory immunologic tests, but they have not been widely adopted because the antibody needed to produce a reaction with the AU-HAA present in the blood is in short supply.

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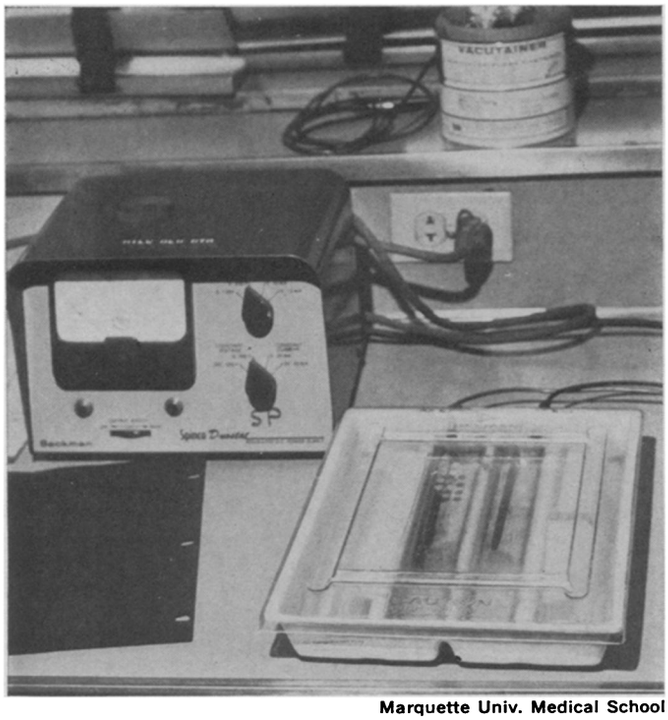
Holper: Proposes thorough screening.

In the gel diffusion test the antibody and blood sample are put into separate test wells and diffuse toward each other through a thin gelatin layer on a glass plate. If the antigen is present it reacts with the antibody, and a white opaque line appears on the plate.

The complement fixation test is about 20 to 30 times as sensitive as the gel diffusion test, according to Abbott, but it requires more of the test antibody. The complement is an enzyme-like molecule of nine different proteins that help break down red blood cells. A few



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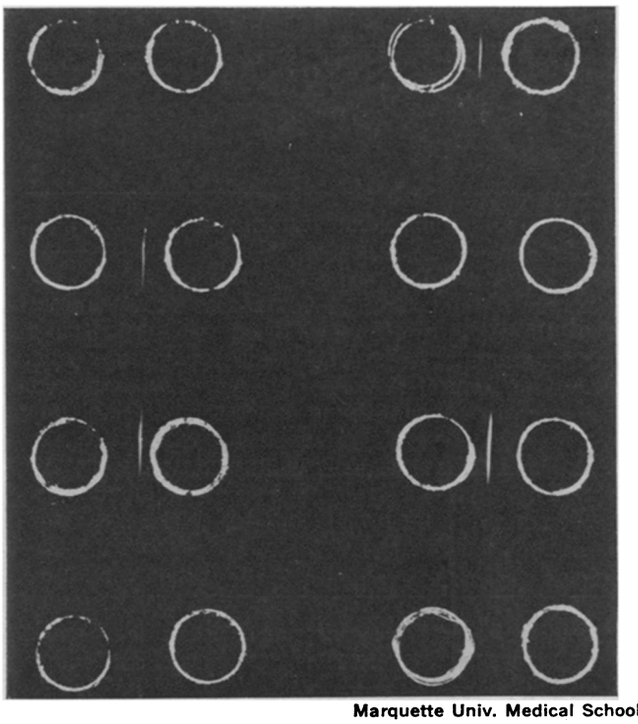
The gel diffusion test is fast and relatively simple.



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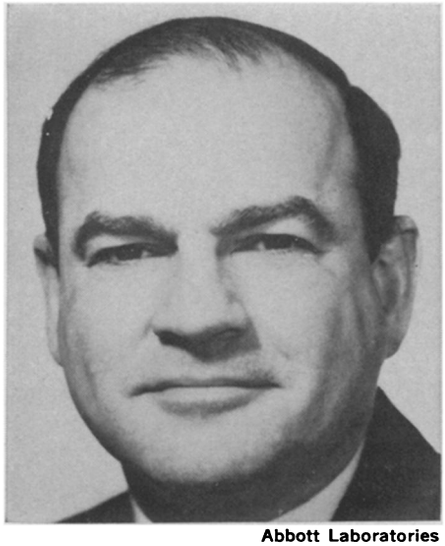
The presence of the antigen is shown by the lines.



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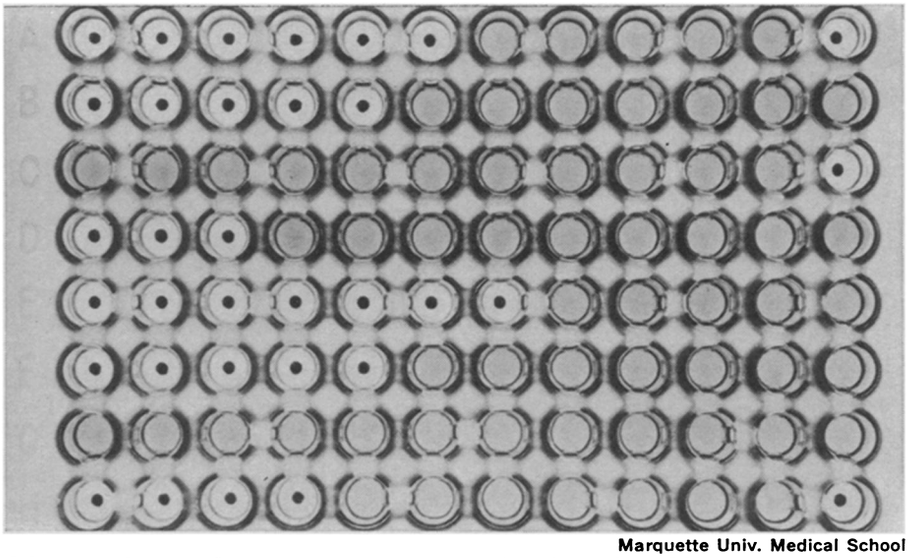
Blumberg: With the antigen, a test.



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The complement fixation test—more complex, but 20 to 30 times as sensitive.

drops of the complement, the patient's serum and sensitized sheep's blood are put into the test wells. The antigen-antibody combination absorbs the complement if the patient's serum contains AU-HAA; the red cells in the sheep's blood do not break down and a bright red button appears. But if the AU-HAA is not present, the red blood cells break down and the test well is almost transparent.

Dr. George M. Kunitake, director of Abbott's Reference Laboratory, says the tests are positive for AU-HAA about a month and a half before standard liver function tests show any abnormality, making it ideal for donor screening. He cites the case of one blood donor who was tested at two-week intervals over seven months; both tests were positive for almost a month and a half before any abnormalities showed up in the liver function test. The donor later developed serum hepatitis. "This sort of experience," says Dr. Kunitake, "convinces us that these tests are a valid screening tool for blood donors and that they can alert physicians to watch patients closely for developing hepatitis."

The tests promise to be an important advancement to blood banking procedure, but thus far the testing systems have been available only as a referral laboratory service. By mid-1970, however, test systems should be available for those clinical laboratories and blood banks that wish to do the tests.

Tests have shown that a patient receiving a transfusion of AU-HAA positive blood has a better than 75 percent chance of contracting hepatitis. The tests are not foolproof, however. "Hepatitis can be transmitted even when both tests are negative," says Dr. Aaron Kellner, director of the New York Blood Center, if the hepatitis virus is dilute.

"This is no excuse to do no testing, for if only one quarter or one half the number of transfusion-induced hepatitis cases can be prevented, the tests are valuable," he declares.

Dr. Kellner estimates that, even using the less sensitive gel diffusion test, the New York Blood Center has prevented up to 1,000 cases of transfusion-induced hepatitis—and 5 to 10 deaths—and claims that there is no point in waiting until tests are perfected for them to provide screening. □