INFORMATION CIRCULAR

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Viral Hepatitis

by

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A. SITUATION IN THE SOUTH PACIFIC REGION

Outbreaks of viral hepatitis have been reported in 13 of the 19 territories of the South Pacific Commission area (no figures are available for the remaining 6 territories) during 1972. The table below shows figures to hand for the months of June, July and August:

Infective Hepatitis Number of Cases	June 1972	July 1972	August 1972
American Samoa	5	-*	19
Cook Islands	9	15	38
Fiji	34	35	23
French Polynesia	3	14	11
Gilbert and Ellice Islands Colony	73	4	4
Guam	16	1	-
Nauru	3	3	1
Condominium of the New Hebrides	6	-*	4
Papua New Guinea	-*	50	32
Trust Territory of the Pacific Islands	8	16	3
Tonga	4	2	1
Wallis and Futuna	1	-*	-*
Western Samoa	8	20	10
Total:	170	160	146

-* No reports to hand for that month.

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In the Cook Islands, a total of 177 cases were reported in the first three weeks of September, and for the last three days of this period there were approximately 20 cases each day. Gammaglobulin prophlaxy is presently being used extensively in the Cook Islands to create passive immunity.

In American Samoa, Dr Lowell Wiese reported some 30 cases of infective hepatitis at the beginning of September 1972, and he has studied, with Dr Rosen (NIH, Hawaii), the epidemiology of this new outbreak. All cases were either former patients of the LBJ Tropical Medical Center (about one month before) or had had professional contact with that hospital. The source of the infection was found to be the drinking water supply of the hospital, in which two people had been bathing, both of whom were Virus A hepatitis carriers.

B. CLINICAL FINDINGS AND BIOLOGY

The term hepatitis designates a diffuse lesion affecting the liver parenchyma as a whole, following an infectious or toxic attack.

Pathological findings are varying degrees of necrosis of the parenchymal cells and cellular mononuclear exudation. The reticulum framework is generally preserved. Healing is by regeneration of surviving cells.

I. Aetiology of Hepatitis:

1. Viral infection is the most common origin of hepatitis.
2. Leptospirosis and bacterial varieties of hepatitis are widespread.
3. Toxic agents, chemicals and drugs are increasingly involved.

II. Types

Type A Virus Infectious Hepatitis may occur sporadically or in epidemics. The liver involvement is a part of a generalized infection, but dominates the clinical picture. It occurs in endemic forms, particularly in warm climates, but major outbreaks can occur due to infected water supplies, poor sanitation and overcrowding at schools and hospitals.

The virus is communicated orally via the intestinal track. It is present in the faeces and blood during the prodromal and acute phases of icteric disease, and in the faeces and blood, in the anicteric form of the disease. Occasionally it is present in an asymptomatic carrier state. The incubation period is two to six weeks.

Type B Virus Homologous Serum Hepatitis:

This infection is transmitted by syringes, needles and above all by blood transfusion. It requires only a minute amount of infected serum or as little as 0.0004 ml to transmit the disease.

Australian Antigen and Hepatitis:

In 1965 in Philadelphia, Blumberg found precipitins in the blood of two heavily-transfused haemophiliac patients who reacted to a single serum antigen, now called "Australian (Au) Antigen". The antigen was identified as a virus-like particle on electron microscopy. Later an investigation at Willowbrook State School, New York, showed that (Au) antigen is the virus of serum hepatitis. In London, Almeida and Waterson (1969) considered the presence of (Au) antigen as "virtually diagnostic of serum hepatitis". The screening of blood donors for hepatitis associated antigen is now routine procedure, using the gel diffusion technique.

Australian Antigens and Antibody in Fijian Serums:

During 1971, 1,211 serums of adults in Fiji were tested for Australian antigen and antibodies using this technique. Of these, 34 contained antigen (2.8%), but there was a surprisingly high proportion with antibodies (6.9%).

Australian Antigens in serums of Natives of the British Solomon Islands Protectorate:

Of 623 serums tested, 85 (13.4%) contained antigen. The findings indicate that the agent responsible for antigenaemia is highly endemic in the British Solomon Islands Protectorate, and that there is a high infection rate in the early years of life.

The hypothesis that mosquitoes (culex) could be biological vectors for (Au) antigen has been confirmed by a recent study of T.A. Smith of Nigeria. It seems that, once infective, the culex mosquitoes remain so for life, because some of the infected mosquitoes that died after eight weeks still had (Au) antigen in their salivary gland.

Serum Hepatitis differs from infectious hepatitis not only in the mode of transmission but in that the incubation period is much longer, ranging from six weeks to six months, and in the presence of Australian antigen,

III. Clinical Findings:

The clinical picture varies a great deal ranging from asymptomatic infection without jaundice to a fulminating disease and death in a few days.

(a) Symptoms:

Infectious hepatitis has remarkably constant symptoms: first a malaise, smokers lose their craving, there is anorexia, vomiting, right upper quadrant pain of the abdomen and tiredness followed by headache and fever (rarely more than 39°C). Diagnosis may not be possible at this stage. Then the urine darkens and overt jaundice and oliguria soon follow. The jaundice lasts one to three weeks (usually 15-20 days), and most patients recover fully.

Variants of this classical form may occur:

(1) The anicteric stage of which the patient may be quite unaware.

(2) The acute fulminant form when the patient may lapse into a coma within a few hours or days.

(3) The cholostatic form - these cases begin as normal infectious hepatitis, but the jaundice does not subside and they soon show signs of biliary obstruction, and biliary cirrhosis may follow. It is the classical protracted catarrhal icterus which is one of the most difficult cases of hepatology to diagnose.

(4) Lastly, the chronic and sub-acute forms, including both cirrhogenous sub-acute atrophy and chronic hepatitis proper. In fact, there are two distinct forms:

(i) curable protracted hepatitis, whose evolution is very slow but which can be cured; and,

(ii) cirrhogenous chronic hepatitis,(active or progressive, which may develop into portal hypertension or liver failure).

(b) Clinical symptoms

Hepatomegaly, usually not serious and which fluctuates from day to day, in over half the cases. Liver tenderness in many cases. There is splenomegaly in 15% of cases and soft lymphadenopathy, especially cervical, may occur.

IV. Laboratory Findings:

The W.B.C. is normal to low and abnormal lymphocytes (virus lymphocytes) may be present. Mild proteinuria is common, and bilirubinuria often precedes the appearance of jaundice. Acholic stools are often present during the initial icteric phase. Liver function tests tend to reflect hepatocellular damage with abnormal cephaline floculation (Hanger test), B.S.P. thymol turbidity (MacLagan test) and transaminase (S.G.O.T. and S.G.P.T.) values. There is a reduction of hippuric acid synthesis and depression of cholesterol esters, increased gammaglobulin and urobilinogenuria. In the cholangiolitic variety, the liver function tests may indicate obstruction as well. A liver biopsy generally shows the characteristic pathology.

Australian antigen is detected by immunodiffusion, electro immuno-adherence and radio-immunoelectrophoresis.

Ouchterlony's immunodiffusion is a simple method which does not require costly equipment. Both reagents, i.e. serum with the antigen and serum with the antibody are dropped into two cupules 5 mm apart on a thin agarose gel smear on a slide. After a diffusion time varying from one to five days in a moist chamber, the antigen and antibody meet and a linear precipitation reaction takes place, easily visible with the naked eye.

V. Differential Diagnosis:

Viral hepatitis has to be differentiated from other diseases that cause hepatitis or involve the liver, such as Weil's disease, amoebiasis, cirrhosis, infectious mono-nucleosis, chlorpromazine intoxication and toxic hepatitis.

In the obstructive phase of viral hepatitis, it is necessary to rule out other obstructive lesions such as choledocholithiasis and carcinoma of the head of the pancreas.

Homologous serum hepatitis is clinically indistinguishable from infectious hepatitis.

VI. Treatment

Rest in bed is necessary until the initial acute symptoms have subsided and should continue to be prescribed until clinical and laboratory evidence of the acute disease have disappeared (jaundice subsides, bilirubinaemia is back to 20 mg and transaminase values to 100 U.). The return to activity during convalescence should be gradual.

A high protein diet is recommended as it seems to reduce the duration of the illness by 20%. However, it may be difficult to absorb early in the illness and the results are not conclusive.

Patients with infectious hepatitis should avoid physical exertion, alcohol and, whenever possible, medecines such as barbiturates, sulfonamides, etc.

If the patient is unable to take or keep food or fluids by mouth, a 10% glucose solution i.v. should be given. If the patient shows signs of impending hepatic coma, protein should be restricted to 40 g/day and increased as the condition improves.

Since there is no anti-viral chemotherapy, cortico therapy is the only alternative. Of course there would be no need for it in ordinary cases which progress to an early recovery. There are four groups of cases when it should be prescribed:

(1) Acute fulminant cases. But it may be ineffective.

(2) Serious cases approaching the stage of pre-coma.

(3) Post-hepatitis cholestasis, where there are signs of biliary obstruction. The dosage of steroids should be reduced very gradually.

(4) If convalescence is prolonged (serum bilirubin $>$ 10 mg/100 ml for two weeks or longer).

VII. Prevention:

(a) Type A Virus Hepatitis

Gammaglobulin prophylaxy is effective in the prevention of viral hepatitis. The doses used vary from 0.04 mg/kg for children who are exposed a short time to 0.12 mg/kg for those exposed longer, adults and pregnant women during an epidemic. It should be administered immediately after exposure since gammaglobulins are ineffective when hepatitis symptoms appear. Preventive action by passive immunity will last one month, but this very costly method will not provide protection to all those treated. It will, however, induce development of attenuated symptoms resulting in the establishment of passive active immunity. Gammaglobulin should be administered to exposed communities, travellers to an infected area and professionally exposed persons.

(b) Standard gammaglobulins are ineffective on B Virus Serum Hepatitis, which is a serious complication of blood transfusion estimated to occur in 3% of transfused cases and up to 12% of mixed plasma transfusions, with a mortality of 0.9%.

Therefore the transmission of viral hepatitis by blood and its by-products must be prevented by:

- systematic detection of carriers of type B virus;
- retrospective investigation of all cases of serum hepatitis;
- search for immunized donors who can provide antibodies for passive immunization;
- elimination of donors with Australian antigen.

Immunization

1 - Passive immunization with anti (Au) gammaglobulin.

After accidental contamination, gammaglobulin from plasma rich in Australian antibodies should be injected as soon as possible.

2 - Research on active immunization carried out simultaneously in France and the United States of America in 1970, shows that the best prospects with regard to infectious hepatitis lie in isolating the virus and in its culture. Heated (Au) antigen has protective properties because heating considerably reduces its contaminating capabilities but does not prevent the formation of antibodies. It is to be hoped that in the not too distant future a vaccine will be available and infectious hepatitis and serum hepatitis will become preventable diseases.

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