ACUTE HEPATITIS: TOXIC OR VIRAL?

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THE HIGH incidence of viral hepatitis, both the infectious hepatitis (I. H.) and the homologous serum type (H. S.), in service personnel during World War II led to extensive studies on the epidemiology, pathology, course and treatment of this condition (1). Data were gathered which were later confirmed by studies on volunteers in whom infectious hepatitis was produced at will (2). These studies also pointed to the fact that the clinical picture of the so called catarrhal jaundice seemed to have been identical in most instances with viral hepatitis. The etiology of catarrhal jaundice appeared solved when the indication for a virus as offender was presented and appeared confirmed with the identification of the virus by Stokes and his co-workers (3).

While there is no doubt that most cases falling into the picture of catarrhal jaundice are of viral etiology there are some cases in which the viral etiology is questionable. This fact is important since thus far the identification of the virus is possible only in selected cases and since some cases of hepatitis, particularly if occurring in the civilian population may have an etiology other than viral, e.g., toxic.

To investigate this possibility the morphologic changes in the liver of proven cases of viral hepatitis (army material) were compared with the morphologic changes in the liver found in many civilian cases of primary hepatitis in a large charity hospital. From these studies morphologic criteria became available to differentiate cases of the viral type of hepatic necrosis from other cases of hepatic necrosis to which the term toxic was applied. Having established the two groups (toxic and viral) on a morphological basis, the results of their clinical and laboratory examinations were then compared and analyzed (4).

In this paper the clinical and laboratory findings of patients suffering from either type of acute hepatitis are presented and their significance in the differential diagnosis of acute hepatitis (viral or toxic) discussed.

MATERIAL AND METHOD

Almost all cases of acute hepatitis which were studied in this hospital for the past 10 years were divided into those of toxic and viral hepatitis respectively. The separation was made in most instances on the basis of morphologic changes in the liver seen in specimens obtained by punch biopsy, surgery, or necropsy. In some it was made on the basis of a specific etiology factor (viral or toxic). The laboratory findings and other clinical characteristics in the history and physical examination of these two groups of cases were tabulated and the similarities and dissimilarities compared.

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Altogether 159 cases of hepatitis with various degrees of jaundice were intensively studied during this period.

HISTORY

In the history receipt of transfusions or injections of blood, plasma, serum, or other blood products within the last 2-6 months was considered as a specific etiologic factor for viral hepatitis. Other therapeutic inoculations or needle punctures for other reasons as in drug addiction were also thought to be significant factors as was also close contact with other jaundiced (hepatitis) patients.

A history of an occupational exposure to hepatotoxic agents (chemicals, drugs, gases, fumes), or treatment with certain hepatotoxic drugs, or excessive intake of alcohol and/or poor nutrition was considered pointing to toxic hepatitis.

In the civilian population toxic hepatitis is not an uncommon clinical entity. Chances to acquire a toxic hepatitis are common in industry, in the home, and in the therapeutic field. Many hepatotoxic substances are now being used in industry, and despite all possible precautions some workers develop jaundice with toxic hepatitis. The most common offenders in this group may be listed under the following headings:

Drugs—Sulfonamides, cinchophen, arsenicals, bismuth and lead preparations, mercurials, anticonvulsants, alcohol, barbiturates, some antibiotics and endocrine substances.

Poisons—Ether, chloroform, phosphorus, carbon tetrachloride, benzene, trinitrotoluene, various other industrial solvents, insecticides and exterminating substances.

In addition to the above specific substances, toxic hepatitis (as noted by liver biopsy) may also occur in association with bacterial and parasitic infections, abnormal metabolic and degenerative processes in the body.

PHYSICAL EXAMINATION

In the physical examination particular attention was given to the general appearance and behavior of the patient (i.e. his mental state), to the presence of fever, chills, sweats, and tachycardia, to the degree and tint of the icterus, and to the appearance of the sclerae and conjunctivae. The size, consistency, and feel of the liver and spleen and the presence of adenopathy were carefully determined. Search was also made for the presence of cardiopulmonary disorders or signs of chronic disease of the gastrointestinal tract, for the presence of edema, ecchymoses, perleche, spider nevi, palmar erythema, pectoral alopecia, gynecomastia, ascites, atopic dermatitis, and hypogonadism.

LABORATORY EXAMINATIONS

In addition to the routine laboratory procedures, the following determinations of hepatic tests were done one or more times according to methods described in a previous paper (5):

Sedimentation rate	Thymol turbidity
Serum total protein	Total serum bilirubin
Serum albumin	Indirect bilirubin
Serum globulin	Prompt direct (1 minute) bilirubin
Serum N. P. N.	
Alkaline phosphatase	Prothrombin time before treatment
Total cholesterol	
Cholesterol esters	Cephalin cholesterol flocculation test
Urine bile pigments	
Urine urobilinogen	Stool urobilinogen

Gamma globulin turbidity

Furthermore in 122 cases one or repeated liver biopsies were performed and the specimens were studied histologically in sections stained by various methods. In 14 cases the liver was studied after the necropsy and 2 cases had both punch biopsy and necropsy.

Fifty patients were followed up to seven years and whenever practicable hepatic tests were repeated. Sixteen patients were readmitted to the hospital for various medical reasons, and in these further liver studies were done. Five female patients were admitted during this time to the obstetrical wards of the hospital and they too had repeated liver function tests.

PATHOLOGY

The biopsy or necropsy diagnosis of either type of hepatitis was made on the basis of the following criteria:

Viral Hepatitis: In early cases, patchy, diffuse, centrally accentuated liver cell damage is noted, the degree varying with the intensity of the disease. There is almost complete absence of fatty changes. There is marked proliferation of the Kupffer cells and infiltration by round cellular elements in the lobule and portal triads. Segmented neutrophilic leucocytes are hardly found. Regeneration of the liver cells is frequent, especially in the periphery of the lobules. Cells with diffusely eosinophilic cytoplasmic bodies and with pyknotic nuclei but sometimes without nuclei are found usually separated from the liver cell plates. They simulate Councilman bodies.

In older cases, liver cell damage may be completely absent and Kupffer-cell mobilization with dense histiocytic infiltration of the portal triads is present where a number of lipofuscin pigments are seen.

Toxic Hepatitis: Here the liver cell damage is zonal and is indicated by various stages of coagulation necrosis. Fatty metamorphosis is usually slight. The periportal triads may be free of cellular infiltration but in the sinusoids some histiocytic elements and dense infiltration with segmented leukocytes are found. The liver damage in general is out of proportion to the bile stasis and severe liver damage with little bile stasis may be seen. Necrosis of the liver cells in the center of the lobules differentiates this form of fatty metamorphosis from simple fatty liver.

CLINICAL OBSERVATIONS

Etiologic Factors

Sex, Race and Age: Of the 159 patients studied, 54 were classified as belonging to the toxic and 105 to the viral group. In the toxic goup, there were 35 males and 19 females; in the viral group, 48 males and 57 females. In the former (toxic) group there were 24 whites and 30 colored while in the latter (viral) there were 27 white, 77 colored and 1 other, respectively. The ages of these patients ranged from the second to the eighth decade in both types, although the younger age groups predominated in the viral form (Table 1). The youngest patients were 19 in the toxic and 16 in the viral type, the oldest 75 and 82 years, respectively.

Precipitating and Predisposing Factors: In the *toxic group* a significant number of patients had a history of exposure to one of the many hepatotoxic substances either from ingestion (drugs, etc.) or from occupational hazards—by inhalation or skin absorption. Cinchophen, arsenic, and barbiturates were the most commonly ingested drugs while the trinitrotoluenes, benzenes, etc. were the most commonly encountered ones among the occupational hazards. Alcohol was a predisposing factor in a moderate number of cases. Pneumococcic and other bacterial infectious processes were the probable causative factors in others.

In the *viral group,* 47 had histories of having received transfusions of blood or blood products within the past six to eight months. "Homologous serum hepatitis" proved to be common also in drug addicts (6), so that an increasing number of young heroin addicts are being admitted with this disease. In confirmation with other reports (7) we also observed instances of viral hepatitis following tattooing, the use of mumps convalescent serum and of topical thrombin, and also among workers in blood banks, in plants dealing with processing of plasma or other blood products, and in clinical laboratories. In one patient serum hepatitis occurred following the injection of influenza vaccine.

TABLE I

DIFFERENCES IN PERCENTAGE INCIDENCE OF AGE GROUPS, SEX AND RACE IN THE TWO FORMS OF HEPATITIS

Disease	Age Group							Sex		Race		
	-20	20-29	30-39	40-49	50-59	60-69	70+	Male	Female	White	Color	Others
Infect. Hepatitis	11.4	52.4	12.4	10.5	5.7	3.8	3.8	45.7	54.3	25.7	73.3	1.0
Toxic Hepatits	1.8	20.4	29.6	20.4	13.0	9.3	5.6	64.8	35.2	44.4	55.6	0

SYMPTOMATOLOGY

While most patients with acute hepatitis had, on admission to the hospital, certain specific complaints and findings in common, some of these symptoms seemed to be more pronounced in one form than the other. A careful analysis of the presenting complaints and findings in these cases of acute hepatitis revealed certain differences in the severity and in the incidence of some symptoms and signs which help differentiate the two groups of hepatitis.

Toxic Hepatitis—Subjective Findings: The toxic form was often ushered in by fever, chills, and headaches, as would be expected from the occasional underlying basis, e.g. pneumonia or other infections. The patients complained of various degrees of abdominal pain, nausea, vomiting, anorexia and distention. Some complained of associated symptoms referable to the chest or heart or kidneys. Diarrhea was also not infrequent. Many complaints were secondary to the toxic substances responsible for the disease and overshadowed the hepatic symptoms. The symptoms may persist for days after admission.

Infectious Hepatitis—Subjective Findings: In the prodromal stage, these patients presented mainly an influenza-like picture as manifested by feverishness, chilliness, anorexia, nausea, occasionally vomiting, malaise, headache, fatigability, muscular aches, flatulence, and soft stools. A marked distaste of food and cigarettes was present in some (8); in others, urticaria, herpes labialis and arthralgia was present. Occasionally, epigastric or upper abdominal distress (severe enough, at times, to simulate as acute abdomen) was prominent while in some chills and temperatures of 103-104 were found. Jaundice was often very slight and the color of the excreta (urine and feces) had not changed perceptively enough to the lay observer.

In the icteric state, the patients complained more of the jaundice and changes in the color of urine and feces. They also complained of gastrointestinal symptoms—anorexia, nausea, and vomiting, and were listless and fatigued. Anorexia persisted in some even after the nausea and vomiting had disappeared.

Some patients, however, were almost symptom-free and entered the hospital merely because of the yellow discoloration in their eyes and skin.

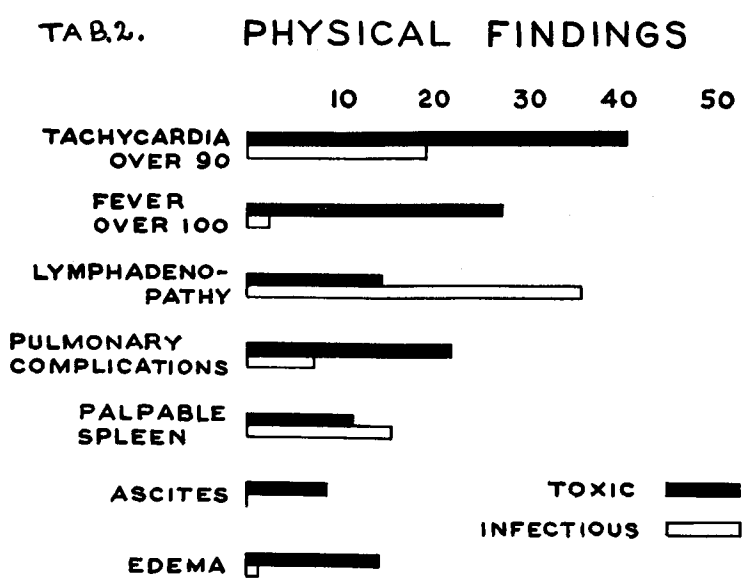
Toxic Hepatitis—Objective Findings: These patients were usually older and appeared as a rule, much sicker than those with the infectious type. They seemed "toxic," hypohydrated, apathetic or lethargic and some occasionally delirious. Bradycardia was rare; there was usually a rapid pulse rate associated with fever over 101 (Table 2). Signs of associated or causative disease in the pulmonary or cardiorenal systems were occasionally present. The icterus was fairly severe and usually of reddish tint, if the patient was seen early. The liver was usually enlarged, smooth and moderately tender to pressure. Edema and ascites were common. Cervical adenopathy and splenomegaly were rare. Toxic dermatitis was occasionally seen.

Viral Hepatitis—Objective Findings: Patients with viral hepatitis were usually younger. Many of them did not appear very ill and seemed to have entered the hospital chiefly because of the jaundice. Rarely, they appeared very ill, mentally disturbed or comatose.

These patients exhibited all degrees of icterus, with a reddish to greenish tint depending on the amount of intrahepatic obstruction, but more commonly showed severe icterus than the toxic group. In some mild pruritus was present initially. Fever of over 101 and pulse of over 90 were comparatively rare (Table 2). Signs of upper respiratory infection were present in the acute form; in some of them injection of the scleral conjunctiva was noted.

Cervical adenopathy was frequently noted, especially in the posterior chain, and at times, the glands were enlarged to a degree suggestive of infectious mononucleosis. This adenopathy was more common in infectious hepatitis than in serum hepatitis.

The liver varied in size, but it was usually tender



Percentage incidence of abnormal clinical findings in the two types of hepatitis.

on palpation and especially on percussion. Characteristically, a dull ache persisted in the liver region for some hours after percussion. Pressure on the liver in the right costo-vertebral angle elicited tenderness in some. The spleen was commonly enlarged but usually was not tender. Ascites and edema were rare, while associated signs of cardiac and pulmonary disease were extremely rare. (Table 2).

LABORATORY RESULTS

While most of the patients with acute hepatitis had abnormal hepatic tests, certain tests were more frequently abnormal in one group than in the other and certain combinations of tests occurred more commonly in one of the two groups. It should be noted that only the results of the initial tests were used in the diagnostic evaluation of these cases.

Toxic Hepatitis:

In these patients the hemoglobin was usually below 50 per cent, the white blood count over 10,000, and the polymorphonuclear leucocytes over 85 per cent; macrocytosis and lymphocytosis were not common. The urine contained 3 plus to 4 plus albumin and 4 plus urobilinogen in a moderate number of cases. Four plus bilirubinuria occurred in about half of the cases, the remainder having smaller amounts of bilirubin in the urine (Table 3).

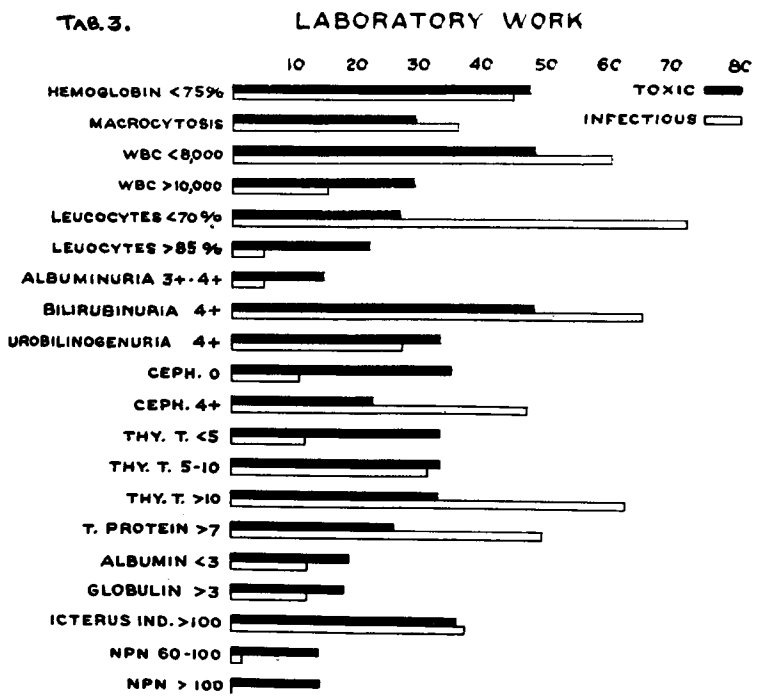
The flocculation and turbidity tests were less commonly strongly positive in this group. Thus, only 46 per cent of the cases had a 3 plus or 4 plus flocculation as against 54 per cent which had 0 to 2 plus flocculation. Similarly 33.3 per cent had a thymol turbidity of less than 5 units and 33.3 per cent had one of over 10 units. Total protein values were, as a rule, lower in this group, as also were the albumin values. The alkaline phosphatase was less than 5 Bodansky Units in 27 per cent of the cases. The cholesterol esters were markedly decreased in this group with 36 per cent of the cases having values of less than 50 per cent and 7 per cent of them having less than 25 per cent esters. Another striking fact was the incidence of high nonprotein nitrogen values in this group. Fourteen per cent had N.P.N. values of 60-100 and 14 per cent of over 100 mg. per cent.

Viral Hepatitis:

These patients had, as a rule, higher values for the red blood count and hemoglobin, and lower values for the white blood count and polymorphonuclear leucocytes. More than half of them had a white blood count below 8,000 (12 per cent below 5,000) and polymorphs below 70 per cent (11 per cent below 50 per cent). The lymphocytes and monocytes were usually increased, the blood smear occasionally simulating that of infectious mononucleosis. Macrocytosis was common. Thus, the blood picture commonly seen in cases of viral hepatitis was that of leucopenia with lymphocytosis and monocytosis and a slight macrocytic, hypochromic anemia.

While marked bilirubinuria and urobilinogenuria were frequent, a 3 plus or 4 plus albuminuria was very rare (4.3 per cent).

The flocculation and turbidity tests were strongly positive with 75.4 per cent having 3 to 4 plus cephalin flocculation tests. Sixty-two per cent of the patients had a thymol turbidity above 10 with values up to 30. Only a small number had an albumin below 3 grams per cent. High values for the icterus index were somewhat more common in this group as also high values for the alkaline phosphatase. Only about



Percentage incidence of abnormal laboratory results in the two types of hepatitis.

one-third of the cases had cholesterol ester values of less than 50 per cent and hardly any a nonprotein nitrogen of over 60 milligrams per cent (Table 3).

TEST GROUPINGS

In addition to the above differences in the results of individual hepatic tests, certain groups of tests appeared to be more characteristic of one than of the other type of hepatitis. Thus, a high bilirubin was commonly associated with a high thymol turbidity in the viral group, but with a moderately elevated thymol in the toxic group. Similarly, a high sedimentation rate was usually accompanied by a high thymol turbidity in the viral group, and by a moderate elevation in the toxic group. Finally, a 3 or 4 plus cephalin was generally present in the toxic group only with marked icterus, while in the viral form, it sometimes occurred with moderate icterus.

CLINICAL COURSE

Toxic Hepatitis:

These patients, while quite ill and, at times, delirious during the height of the disease, usually improved moderately rapidly once the acute stage was over. The gastro-intestinal symptoms disappeared, appetite returned and the general condition improved. The icterus cleared fairly rapidly at times, seemingly from day to day the liver decreased in size and the patients were soon anxious to leave the hospital.

Some patients, however, particularly those with a severe associated disease, remained desperately sick for a long time before recovery or death ensued. Even when comatose, some recovered with successful treatment of the underlying toxic factor, in contrast to patients with viral hepatitis who succumbed within a few days once cerebral symptoms had appeared. Clinical improvement seemed to become apparent before striking changes were noted either in the hepatic function tests or in the morphologic appearance of hepatic biopsy.

Viral Hepatitis:

These patients generally had a somewhat less stormy but more prolonged course than those with toxic hepatitis. Those who entered following a mild upper respiratory prodromal syndrome had few symptoms and improved rapidly, as did their liver function tests. Those who had had marked prodromal symptoms continued to have anorexia, nausea, bloating and upper abdominal distress for some time (7-10 days), and only slowly regained their appetite and general feeling of well being. In some, mild symptoms of aching in the right upper quadrant especially on slight exertion, some anorexia, food selectivity, distaste for fatty foods with associated fat intolerance, feeling of fatigue, and vasomotor disturbances persisted throughout the hospital stay, even after disappearance of jaundice.

Patients who continued with symptoms of liver dysfunction long after the acute stage had passed gradually went into a stage of chronic hepatitis. They continued to exhibit symptoms and signs of the preceding hepatitis although to a lesser degree.

Another group apparently recovered completely from the original hepatitis, but complained of recurring symptoms after varying intervals. These recurrences seemed to be brought on by such factors as physical overactivity, excess of food or drink, exposure to hepatotoxins, inclement weather or intercurrent infection. The frequency and severity of these recurrences depended upon the inciting factors. In some of the female patients, pregnancy and the puerperium caused recurrence of certain symptoms. Occasionally, no apparent inciting factor was present.

PROGNOSIS

The two types of hepatitis also differ from the prognostic point of view. The toxic group had a mortality of 24.1 per cent, while of the 14 patients followed up, only two complained of weakness. One of these was later readmitted as a possible gall bladder disease. One patient was later readmitted as a bronchopneumonia and expired.

In the viral group the mortality was 7.6 per cent while "liver" symptoms (anorexia, weakness, dull right upper quadrant ache, fatigue, etc.) persisted in over 50 per cent of those who attended the gastro-intestinal clinic. Two patients had to be readmitted to the hospital because of these symptoms but recovered again and left the hospital.

DISCUSSION

Clearly, the most important differential diagnosis in the icteric patient is between jaundice due to primary hepatitis from that due to extra-hepatic obstruction. However, at times it is also important to decide whether the hepatitis is toxic or viral in origin inasmuch as differentiation between the two types is frequently of practical therapeutic importance. The clinician should recognize the two types of primary hepatitis and be aware of the fact that labeling every jaundice case not due to an extra-hepatic obstruction as viral hepatitis is occasionally as objectionable as the previous nomenclature of catarrhal jaundice. While patients with a definite history of carbon tetrachloride or chloroform poisoning will often be correctly diagnosed as toxic hepatitis, it is emphasized that there are other cases of toxic hepatitis in whom the etiologic toxic factor must be carefully and often tediously elicited.

Toxic hepatitis differs from the viral type regarding incidence (9) (seasonal, localities, epidemics), frequency and predominance in certain groups (racial, sexual and age). The subjective symptoms, physical findings, laboratory results, findings on liver biopsy or necropsy specimens, clinical course and outcome are different in toxic hepatitis. These differences are, at times, poorly demarcated and a differential diagnosis can be made only later in the course of the disease. Thus, for example, the jaundice developing during arsenical therapy may be either toxic or viral in origin and the differentiation may only be made after an interval when certain symptoms and findings have become more predominant.

As a rule toxic hepatitis is a priori a more serious condition. Most of the patients suffering from toxic hepatitis enter the hospital in a precarious state. At times they are even too ill to give a reliable history on admission. They also show more vividly the results of their complaints—nausea, vomiting, anorexia, diarrhea, fever, etc.—since they appear hypohydrated, lethargic, feverish and at times delirious. Their pulse

is usually rapid and the temperature high, particularly in those in whom the toxic hepatitis is secondary to some pulmonary disease.

While hepatic enlargement is common in hepatitis the largest livers were found in cases of toxic hepatitis. In patients with toxic hepatitis who had an alcoholic background the livers were at times tremendously enlarged, reaching almost to the iliac crest. Very large livers were also noted in two cases of cinchophen ingestion, in one case of carbontetrachloride poisoning and in one case of chronic pancreatitis with acute exacerbation. The large livers of the toxic hepatitis cases appear also more tender to simple palpation than those of patients with infectious hepatitis. This tenderness may at times be severe enough to suggest, in conjunction with the abdominal pain, the likelihood of an acute surgical abdomen, so that surgical consultation was requested in several instances. The hepatomegaly noted in our cases of toxic hepatitis did not decrease when the patients' condition became progressively worse so that at post mortem some livers weighed up to 3000 grams or more in contrast to the small livers, 700-1200 grams of the fatal cases of infectious hepatitis.

The laboratory examinations in toxic hepatitis show pathologic results particularly in those tests which more or less are related to changes in the hepatic parenchymal cells rather than in the mesenchymal (R.E.S.) tissues. Thus the cholesterol esters and albumin are on the average lower in toxic than in viral hepatitis. However, the total globulin including gamma globulin are higher and the flocculation and turbidity tests relating to the gamma globulin are more frequently positive in the viral type of hepatitis. The cephalin flocculation was more often negative and the thymol turbidity low particularly in the toxic hepatitides due to alcoholic debauche. Similarly the association of toxic hepatitis with leucocytosis and high or normal polymorphonuclear leucocyte count was quite striking in comparison with the relative leucopenia and lymphocytosis of the viral type.

That toxic hepatitis is a more serious illness than the viral type may be gleaned from the mortality in these two types, which was 24.1 per cent in the former and 7.6 per cent in the latter one. While in the civilian population of a charity institution representing all ages and all degrees of physical fitness, the mortality of any disease will be higher than in the young patients of the armed services, the differences are nevertheless significant despite the fact that the mortality of 7.6 per cent in our cases of viral hepatitis was much higher than the usually quoted figure of 0.2 - 0.7 per cent. We believe that our 7.6 per cent mortality in viral hepatitis is due to the mortality in patients with homologous serum jaundice which is much higher in a private hospital than in the services because of the nature of the primary condition necessitating blood transfusion.

While the immediate prognosis in toxic hepatitis appears to be more serious than in viral hepatitis the final outlook seems better except perhaps in the alcoholic group. Patients with toxic hepatitis usually improve more rapidly once the convalescence stage sets in and are usually free of symptoms later on. Cases of viral hepatitis, on the other hand, require longer convalescence and are more prone to residual symptoms. Of our cases with toxic hepatitis only a small percentage progressed into the chronic stage. The incidence of chronic hepatitis in the viral type was much higher but this was probably also attributable to the nature of the clinical material—malnourished patients from poor hygienic surroundings, alcoholics, narcotic addicts and older individuals with associated diseases. That viral hepatitis may be more serious in older patients and in those with associated diseases has been accepted by other workers in this field (10).

The insidious nature of viral hepatitis makes prognosis more uncertain than in toxic hepatitis. The dictum "each hepatitis case a potential case of acute yellow atrophy" has been in our experience more applicable to viral than to toxic hepatitis: some patients may appear comparatively well one day, only to become stuporous within 24-48 hours and die within another 48 hours. On the other hand, cases of toxic hepatitis which proceed to hepatic coma and death, usually run a progressively downhill course.

The need for differential diagnosis between the toxic and viral form must be considered also from the therapeutic point of view. While much of the pathologic physiology of viral hepatitis is unknown, present knowledge points to an active process proceeding rapidly to necrosis, disappearance of the liver cells, and, occasionally, collapse of entire lobules (11). In toxic hepatitis, on the other hand, there appears to be a gradual breakdown of the hepatic cells with fatty infiltration and degeneration before necrosis; moreover, the associated or responsible primary disease may affect the hepatic pathology. Hence, in toxic hepatitis, specific therapy is often applicable, while in viral hepatitis, except for the prophylactic use of gamma globulin (12), the treatment is usually only supportive. The specific therapeutic procedures in toxic hepatitis include the use of substances related to enzyme activity (e.g. Bal in hepatitis due to heavy metals), to lipid transport (e.g. methionine and choline in hepatitis associated with fatty liver (13), and for combatting various pyogenic and other infections.

While the advent of the wider spectrum antibiotics—aureomycin (14) and terramycin—and of ACTH and cortisone (15) has somewhat modified the treatment of both types of hepatitis, their best results are still noted in cases of toxic hepatitis.

SUMMARY

Primary hepatitis exists in two forms. These two forms of hepatitis—viral and toxic—present certain differences in their etiology, symptomatology, and laboratory tests.

The clinical course and prognosis vary markedly in these two types of hepatitis. Specific therapeutic procedures are usually present for cases with the toxic type but absent for those with the infectious type.

Differentiation between the two types of primary hepatitis is more than just of academic interest, and hence, it should be attempted in every case.

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