

cholangiogram, the changes of bile ducts were investigated in the living body. In the experimental animals, cirrhosis was produced by CCl_4 , T.A.A and choline deficiency. Also, subacute hepatitis was induced by ethionine feeding. Tritiated thymidine was injected before sacrifice and autoradiographs were prepared. The biliary system was injected with Neoprene latex and the same done with a differently colored material for the portal vein.

(Result) 1) The corrosion casts of normal liver showed the ducts ramified dichotomously into approximately equalized branches for five to six divisions, where the branches were about 150 μ to 250 μ in diameter. From that point on most branches were much smaller than half the parent branch, being on the order of 20 μ to 100 μ . They extended at right angles from the larger branch, although some dichotomous branching was noted even in the terminal branches. No communications were found between ducts either in casts or in thick frozen sections.

2) In the case of postnecrotic cirrhosis with large regenerating nodules, the inflammatory process around bile ductules was severe. The nodules compressed vascular beds, especially hepatic vein. The cast of bile duct appeared denser and more intricate than the normal. Closer inspection revealed an increase in the number of branches beyond the fourth dichotomous divisions, involving principally ducts of less than 250 μ in diameter. Whereas in the central casts small straight branches arose at right angles from the larger branch, in these specimens they originated at random angles and were also tortuous changing direction two or three times. Thick frozen sections demonstrated occasional small communications between adjacent ducts. However, no direct compression by regenerative nodules against bile ducts, as case with vascular system, was found.

3) The cases of diffuse septal cirrhosis (nutritinonal or Laennec cirrhosis) were in all respects similar to those obtained in cases of the postnecrotic cirrhosis, but all variations from the control, such as tortuosity and increase in number of branches, were not so exaggerated. Clinically, the jaundice was less severe than the former case.

4) In the experimental cirrhosis, the course of bile ducts became irregular and independent from the vascular systems. Autoradiographs revealed many labeled epithelial cells of bile duct. The subacute hepatitis exhibited the changes between normal and cirrhosis on overall respect.

(Summary) The obstructive jaundice seen in cirrhosis is due to irregular proliferation of bile duct instead of the direct compression by regenerative nodule to the vascular bed.

4. A PEDIATRICAL STUDY OF CHOLESTASIS

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In this study, the authors and his co-workers classified cholestasis occurring in children into two major divisions, intrahepatic cholestasis and extrahepatic cholestasis which were further sub-divided as show in Table 1.

The present paper deals in particular with the cholestasis in infancy, focussing stress on the study performed by the authors.

1) Intrahepatic cholestasis:

As used in this paper, the term "infantile hepatitis" is a general name for the incomplete obstructive jaundice which is found infants. Although the cause for the disease is yet to be elucidated, it is believe to be of multiple factors. At present, however, all the researchers do not necessarily share the same view of this cause.

The authors make it a rule to give the name "infantile hepatitis, Type I" to those with which no hepatic dysfunction other than jaundice is observed and the name "infantile hepatitis, Type II" to those with which any hepatic dysfunction is observed. With the infant hepatitis, Type II, particularly bilirubin-mono-glucuronide shows a high value in the serum bilirubin fraction, both the serum GOT and GPT values are elevated, and a slight obstruction is recognized in the colloid reactions.

As regards the prognosis, the infantile hepatitis, Typ I, is generally satisfactory, with the disappearance of recognizable symptom within 3 months on the average. By contrast, the infantile hepatitis, Type II, is divided into two groups, one with satisfactory prognosis and the other with inferior prognosis. At any rate, it is difficult to make a precise judgement as to the prognosis on Type II at an early stage of disease.

Among cases of infantile hepatitis, Type II, some are found to have giant cells and others to lack them through histopathological examination. As will be discussed later on, however, the giant cells cannot be concluded as being recognized peculiarly in the infantile hepatitis.

Among infantile hepatitis, Type II, whose prognosis is inferior, there are some which experience repeated occurrence of nephropylitis, which eventually transforms into biliary cirrhosis of the liver.

It is generally difficult to make a precise diagnosis of viral hepatitis in infancy, and there are rare cases which manifest typical symptoms. Although there are quite many cases which receive exchange transfusion because of incompatibility of blood types such as of Rh and ABO in the neonatal period, very few reports are available dealing with cases that suffer from occurrence of serum hepatitis due to such transfusion.

The authors have an experience of treating a newborn infant who, upon diagnosis for incompatibility of blood type of ABO immediately after birth, received exchange transfusion of 600 ml of preserved blood and, on the third month of birth, was observed to be suffering from swelled liver. In this particular case, the systemic conditions on the third month of birth did not show pyrexia, displeasure or similar abnormality, but a hard swelling of liver of a length about 5 cm could be felt, the serum GOT and GPT values was elevated, and the colloid reactions were positive. Thus, the authors diagnosed this case, with some doubt, to be a serum hepatitis. However, this case showed a total serum bilirubin value below 3 mg/dl and manifested an inconspicuous extent of jaundice.

The microscopic tissue image of this cases as observed for pathological study showed a remarkable infiltrations of lymphocytes, and potty necrosis of liver cells at Glisson's capsule and at the center of the lobes, but no giant cells could be detected.

After about 3 months' treatment, this case achieved alleviation and was released from the hospital. It is now under a followup observation.

As an example of toxic hepatitis, the authors have an experience of treating a patient who, in the course of infantile hepatitis, Type II, was orally misapplied about 30 ml of 0.1% ethyl mercury sodium thiosalicylate (Mersonin) and, as a consequence, had her hepatitis aggravated. Aggravated symptoms were total serum bilirubin value which rose about twice as great, the serum GOT and GPT values which both rose about 4 times as great, and swelled liver which increased in size. These symptoms were alleviated invariably through treatment.

Furthermore, the authors have an experience of treating a pair of sisters suffering from Rotor's hyperbilirubinemia. The elder sister was 7 years old, and the younger sister 5 years old, and both were observed to have chronic latent jaundice. So far as findings of examination are concerned, no conspicuous abnormality was observed excepting a relative rise in the conjugated bilirubin values and a delay in the BSP excretion value. No conspicuous abnormality could be detected either from the pathological tissue investigation by many of liver functions test.

2) Extrahepatic cholestasis

The authors have an experience of treating a total of 15 cases of congenital atresia of the bile ducts. Of this many cases, 10 cases were of female patients. Where the time of occurrence of disease is concerned, 8 of the 15 cases were of jaundice which followed physiologic neonatal jaundice. However, the remaining 7 cases, although physiologic neonatal jaundice disappeared once completely, complained of jaundice which returned after an interval of from 7 days to 47 days. All these cases were reported to have feces yellow in color before the recurrence of jaundice.

This suggests that there is a possibility of some, but not all, bile ducts being closed after

birth. From a different point of view, such cases may be concluded as being included in the group possessed of a congenital predisposition toward atresia of the bile ducts.

In accordance with the method of classification proposed by Gross, conditions of atresia of the bile ducts were composed of 4 cases of Type I, none of Type II, 1 case of Type III, 7 cases of Type IV, 1 case of Type V, none of Type VI and 2 cases of Type VII so far as the cases treated by the authors are concerned. It was only in one of the cases of Type I that complete cure was achieved by resorting to surgical operation.

Clinical findings of the 15 cases of congenital atresia of the bile ducts are shown in Table 2. In the first month of birth, jaundice and swelled liver were observed; in the second month, rise of serum GOT and GPT values was noted; in the third month, swelled spleen was conspicuous; and in the fourth and following months, appearance of ascites and dilation of the abdominal wall veins were found.

Some workers advance a theory that appearance of giant cells in the livers of the patients of infantile hepatitis is caused by viral infections. According to the experience of the authors, however, appearance of giant cells was also observed at a high ratio in livers of the patients of congenital atresia of the bile ducts other than in infantile hepatitis. On the other hand, it was not observed in said case of doubtful diagnosis of serum hepatitis. From this, the authors have concluded it impossible to attribute the cause of giant cells only to viral infections. Although the cause in question is yet to be investigated further, the authors believe it recommendable, at least for the moment, to refrain from adopting the diagnostic title "giant-cell hepatitis of pathologic tissue study" for clinical diagnosis.

These giant cells showed a trend toward disappearance as either biliary cirrhosis or fatty liver intensified.

It is interesting to note the fact that occurrence of hepatic rickets was observed only in cases of infantile hepatitis, Type I and Type II, and cases involving the transformation of Type II to biliary cirrhosis, and was not observed in cases of congenital atresia of the bile ducts.

In case of cholestasis occurring in children, especially in young infants it is one of the important factors to make an early differential diagnosis among congenital atresia of the bile ducts, infantile hepatitis, Type I, Type II and viral hepatitis. As shown in Table 3, the authors have achieved significant results in such diagnosis by repeating the examination for serum bilirubin-mono-glucuronide concentration %, serum GPT and serum beta-glucuronidase with intervals of about 2 days in the course of treatment and by conducting follow-up observation closely.

Now the authors wish to discuss a part of the problem demanding particular attention from the standpoint of diagnosis of cholestasis in infancy, referring to the following two cases:

Case 1: This patient, in her tenth month of birth, was diagnosed by a certain physician to be a case of congenital atresia of the bile ducts in view of such symptoms as jaundice, swelled liver and white feces.

The authors, after observing an excretion of thin bile through examination of her duodenal juice, administered 0.2 g of dehydrocholic acid as a daily dose continuously for a week. As the consequence, the color of feces changed from white to yellow and the jaundice disappeared, enabling the patient to be released from hospital for complete alleviation within about one month of diagnosis. In this particular case, the authors used "infantile hepatitis, Type II" as the clinical diagnostic name for the case. This was a case of excellent prognosis.

Case 2: This patient was said to have had yellow feces for the first 20 days of birth but, in about one month of birth, began to manifest occurrence of jaundice and excrete light yellow feces. Upon such complaints, a certain hospital conducted I¹³¹ Rose-Bengal test with negative result of atresia of the bile ducts. Moreover, because the diagnostic name "giant cell hepatitis" based on the pathologic tissue study findings through liver functions test was adopted, as it was, for the name of clinical diagnosis, the patient was treated as a case of infantile hepatitis.

By reason of aggeravated disease, the patient was sent to our hospital when she was in his fifth month of birth. Based on the observations that the total serum bilirubin value was 20 mg/dl and the feces had a low bile concentration, the authors diagnosed her to be a case of congenital atresia of the bile ducts. Results of surgical operation performed on this case belonged under Type IV according to Gross' classification.

In view of this particular case, the authors wish to warn against ready adoption of the diagnostic name "giantcell hepatitis" due to the pathologic tissue study as the clinical diagnostic name without forming a comprehensivs judgement by taking into account other clinical findings.

5. CHOLESTASIS

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I will describe the outline of the surgical management of cholestasis and also few points of pathophysiology, which were observed and confirmed during the operation.

1) Surgical management for cholestasis is mainly subjected to the extrahepatic obstruction of the bile duct causing hindrance to the bile flow.

The subject on cholestasis which occurs secondary to cholelithiasis shall not be discussed since this condition can be easily treated by the operative intervention of cholelithiasis itself.

A total of 157 clinical cases, of which 68 cases were experienced from 1955 to 1964 by the staff members at the first department of surgery of Kyoto University Hospital and also 89 cases which were done exclusively by the author and his colleagues at the second surgical department of Kanazawa Medical School from 1959 to 1965, are reviewed in this paper.

Diseases discussed here are mostly the cases of obstructive jaundice due to malignant tumor arising from the areas surrounding the extrahepatic biliary tree (142 cases and 90.4%) such as cancer of the common duct, pancreas, ampullary region and the region of hepatic hilum and also metastatic gastric cancer. In addition to these diseases, the less numbers of benign ones (15 cases and 9.6%), namely postoperative biliary fistula, congenital biliary atresia and idiopathic choledochus dilatation, are included.

At first, the operative methods are classified roughly into two groups, namely the one in which extrahepatic bile duct can be used and the other in which not.

In the first group, the gallbladder, common duct and common hepatic duct are used to make anastomosis with the jejunum or duodenum. Besides, in some of the cases, either one of the left or right branch of hepatic duct is utilized.

In the second group, for the cases in which the extrahepatic bile duct is not able to be used, the method of inserting T tube into the bile duct, hepatoenterostomy or transhepatic intrahepatic bile duct drainage are applied instead.

In giving more detail of these each operative method, the anastomosis between the gallbladder and the intestinal tract can be constructed with much ease technically. This type of anastomosis has been used most frequently in the past since this method has given satisfactory results to relieve jaundice when it is used on indicated cases. Jejunum has been used most frequently as a partner in this type of anastomosis.

There are two ways in this type anastomosis, one of which is the cholecystojejunostomy supplemented by Braun's anastomosis and the other is so called Roux en Y type of anastomosis. Former method is much simpler technically, but the latter will be the method of choice theoretically from the point of preventing ascending infection. It is not necessary to be too conscious of the Roux en Y anastomosis technique, since there has been no significant difference observed between these two types of anastomosis as far as the incidence of ascending infection is concerned.

Cholecystojejunostomy itself is also an impractical procedure in the cases of either the presence of cystic duct obstruction or if the cystic duct is very long and jointed to the common duct near to opening of the duodenum. Application of the gallbladder at the time of reconstruc-