Jaundice of Pregnancy

Obstructive cholestatic jaundice appearing in the last trimester of pregnancy has been called idiopathic hepatopathy of pregnancy,1 hépatite bénigne de la grossesse,2 and idiopathic jaundice of pregnancy.3 Perhaps recurrent intrahepatic cholestatic jaundice of pregnancy is the most appropriate term.4 5 Many patients experiencing generalized itching in the last weeks of pregnancy may be suffering from this condition, for jaundice is rarely deep and may be inapparent. So the physician should seek evidence of dark urine and pale stools. After delivery pruritus ceases, and in one to two weeks the jaundice disappears. The condition is apt to recur in subsequent pregnancies.

The serum shows an increase in conjugated bilirubin and alkaline phosphatase. Serum transaminase levels are normal or slightly increased, but occasionally very high values are found. Needle biopsy of the liver shows mild focal and irregular bile stasis. Hepatocellular necrosis and cellular reaction are absent. Electron-microscopy shows the dilatation, blunting, and swelling of the microvilli which is constantly found in all forms of cholestasis.6 The jaundice is probably due to an unusual cholestatic reaction to a steroid produced in pregnancy. Whether this is an unusual response to a natural steroid or caused by the production of an unknown cholestatic steroid remains uncertain. Changes in oestrogen metabolism are more likely to be secondary to the jaundice and the circulation of oestrogens in the liver than a primary defect.7

Normal women in the last trimester show increased difficulty in transfer of the test substance bromsulphalein into the biliary canaliculi. Bilirubin is in many ways analogous to bromsulphalein, and the response in recurrent cholestatic jaundice of pregnancy may be an exaggeration of the normal one. Moreover, natural oestrogens in large doses also cause abnormalities in the transfer of bromsulphalein.8 There is also an association between jaundice after administration of an oral contraceptive and the intrahepatic cholestasis of pregnancy. About 100 cases of jaundice from oral contraceptives have been reported. In the largest series, 50 Chilean patients, the clinical, biochemical, and microscopical findings bore a strong resemblance to those of cholestatic jaundice of pregnancy.9 Forty of these 50 patients had previously been pregnant, during which 17 had suffered jaundice and pruritus and ten late pruritus only. Oral contraceptives cause a fall in bromsulphalein transport when given to normal non-pregnant women,10 and they may produce the histological appearances of intrahepatic cholestasis.11 A familial incidence has been reported in relation to one patient who was affected by recurrent intrahepatic cholestasis of pregnancy and who developed cholestasis when given an oral contraceptive.12 Her mother and her sister also suffered pruritus and jaundice in pregnancy. It is interesting that reports of jaundice after oral contraceptives come from such regions as Chile and Scandinavia, where recurrent intrahepatic cholestasis of pregnancy is also common.13
Oral contraceptives should not be given to patients who have previously suffered pruritus in pregnancy, and special care in the prescribing of them should be taken in countries where intrahepatic cholestatic jaundice of pregnancy is frequent.

In a woman's first pregnancy the differential diagnosis of idiopathic cholestatic jaundice from viral hepatitis and other conditions causing jaundice may be difficult. It might be possible to perform a diagnostic test after delivery. Serial serum-bilirubin, alkaline-phosphatase, and bromsulphalein tests are done before, during, and at the end of a one-cycle course of an oral contraceptive drug in standard dosage. Increasing cholestasis would confirm the diagnosis of intrahepatic cholestatic jaundice of pregnancy, contraindicate further use of this method of contraception, and give warning that subsequent pregnancies might be complicated by intrahepatic cholestatic jaundice. Differential diagnosis must also be made from surgical jaundice. In some cases laparotomy has been undertaken, because of the unusually long duration of jaundice and a preceding history of operation for gallstones. In a recent well-documented case report the liver was found not to be enlarged, but greatly dilated bile capillaries were visible on its surface. Cholangiography showed a normal appearance, and the amount of bile secreted, the secretion pressure, and its viscosity were found to be within normal limits. The patient subsequently had a normal spontaneous delivery, and the child was healthy. The aetiology of this condition is unknown, but the prognosis is nevertheless excellent. In this patient the jaundice disappeared within three weeks and hepatic histology returned to normal within three months of delivery despite the persistence of jaundice for six months of the pregnancy.

There are certainly many other cases of jaundice during pregnancy, for it has been estimated that it complicates one of every 1,500 gestations. Sexual hepatitis accounts for two-fifths of cases, intrahepatic cholestasis for one-fifth, and obstruction of the common bile duct for one in 20. The acute fatty liver of the third trimester of pregnancy is a condition observed particularly in the malnourished patient with pyelonephritis treated with a tetracycline. The liver cells contain multiple fat droplets without significant necrosis or cellular infiltrate. The liver in pregnancy, when demands for protein anabolism are increased, may be more sensitive than in the non-pregnant woman to drugs which depress this function, such as the tetracyclines. The biochemical pattern is of increased serum levels of bilirubin, reduced prothrombin time, azotaemia, hyperuricaemia, and acidosis. Serum values of transaminase and alkaline phosphatase are only moderately raised, a point of distinction from virus hepatitis. The prognosis of acute fatty liver of pregnancy is poor and there is no clear-cut course of management; caesarean section has been advocated. Corticosteroids are of no value.

Though tests of liver function in patients with toxemia of pregnancy may give abnormal results, particularly the alkaline-phosphatase and serum-transaminase tests, jaundice is infrequent. It was present in 10 out of 90 cases of toxemia in H. L. Sheehan's necropsy series. It is a grave, terminal sign of haemolysis. Histologically the liver shows periporal deposition of fibrin in the sinusoids, with haemorrhages. Centrilobular necrosis and haemorrhages reflect shock, and an inflammatory reaction is inconspicuous. In eclampsia the damage to the liver is terminal, and toxemia of pregnancy cannot be regarded as primarily involving the liver. Toxaemia rarely enters into the differential diagnosis of jaundice in pregnancy.

Finally, drug jaundice should not be overlooked. Increased sensitivity to tetracycline has been discussed. Other drugs to be borne in mind include chlorpromazine and halothane, while the sulphonamides, novobiocin, and phenacetin should be considered as possible causes of jaundice in immature or premature babies.

### Appointment Systems in General Practice

The growth of appointment systems is one symptom of the reorganization of general practice which is gathering momentum. Dr. Bruce Cardew estimates in a paper at page 542 of this week's *B.M.J.* that a third of all N.H.S. practices are now offering a complete appointment service to their patients. Thus 17,000,000 people can now consult their doctors by appointment. That the new pay system is accelerating the movement is suggested by an increase in the first nine months of this year of 2,773 in the number of doctors using the Lloyd-Hamol appointments diary, but it is noteworthy that under the Pool system 4,500 doctors had been prepared to finance appointment schemes entirely out of their own pockets.

J. M. Bevan and G. J. Draper, of the Oxford University Department of Biomathematics, have recently investigated appointment systems. They had three main objectives: to find out the attitudes of doctors and patients to them; to get quantitative estimates of their effect on doctors' work load and patients' waiting time; and to determine which types of practice would find appointment systems worth while and what were the best ways of organizing them. They formed various theories from interviews with and postal surveys from doctors and patients, and tested them in an experimental study of the records of several practices before and after starting appointment systems. The vast majority of doctors and patients who had used an appointment system were satisfied with it. Nearly all doctors found that it was easy to introduce into their practices, that it evened out the work load throughout the week, and that it decreased the strain of their work and improved its quality. Patients who were elderly or of low intelligence found it difficult at first, especially if they had not been informed beforehand by circulars about its introduction and how to use it, but they liked it once they had got used to it. About half of the doctors who did not have appointment systems at the time of the survey thought them...