*Van Royen, E. A., Ten Cate, J. W. (1973). *Lancet*, 2, 449.

Enzyme Analysis using the Vitatron 'Automatic Kinetic Enzyme System'

P. O'GORMAN, SHANTA PATEL, AND VALERIE A. PARSONS (*Brook General Hospital, London, and Greenwich District Hospital, London*) The Vitatron 'automatic kinetic enzyme system' is a new instrument for automated discrete enzyme analyses by the kinetic method. It possesses the advantages of variable reaction temperature, small sample of neat serum, and automatic calculation of activity with printout of results.

The apparatus has been tested according to the scheme for evaluation of instruments for automatic analysis (*J. clin. Path.*, 1969, 22, 278) under routine laboratory conditions for a series of commonly requested enzymes.

Results of these assays have been compared with those from the existing routine methods and the delivery of two instruments to neighbouring hospitals has enabled comparison of instrument performance.

Electron Microscopical Investigation on Intravascular Coagulation in the Human Renal Glomerulus

J. H. SCHUURMANS STEKHOVEN AND U. J. G. M. VAN HAELST (*Institute of Pathology, Laboratory of Electron Microscopy, University of Nijmegen, The Netherlands*) Out of a total of 230 renal biopsies, studied by electron microscopy, intravascular coagulation was found in 67 biopsies (29%) performed in 58 patients. Of these 67 biopsies, 31 were taken from 24 patients with a transplanted kidney and 36 from 34 patients with various glomerular diseases. In 38 out of the 67 biopsies aggregates without distinct cross striation are found in varying numbers in the capillary lumina of the glomeruli. Real fibrin, ie, with cross striation, was found in eight cases; three different forms could be distinguished. In the remaining number of the cases, the capillary lumen is filled partly or completely with material which shows a great diversity of its ultrastructure; this material has a light floccular or dense aspect. Disintegrating erythrocytes, macrophages, remnants of endothelial cells, and sporadically some thrombocytes can be found in this material. In these cases the normal endothelial lining of the basement membrane has partly or completely disappeared.

By comparative study of sequential biopsies we shall try to answer the question if and to what extent the morphological aspects of intravascular coagulation change with time.

Intravascular Coagulation and Pregnancy

JOHN BONNAR (*Department of Obstetrics, Radcliffe Infirmary, Oxford*) Extensive changes occur in the coagulation and fibrinolytic systems during pregnancy, particularly in the third trimester. The concentration of plasma fibrinogen, factor VIII, factors VII and X substantially increases and plasma fibrinolytic activity markedly decreases. During childbirth changes in keeping with activation of the clotting mechanism take place and fibrinolytic activity returns to normal after delivery of the placenta. The changes in the haemostatic systems in pregnancy may be a physiological development to preserve the integrity of the maternal and fetal circulations during pregnancy and to facilitate haemostasis in the uterus during and after separation of the placenta. These alterations also establish a vulnerable state for intravascular coagulation.

In conditions such as abruptio placentae and amniotic fluid embolism massive intravascular coagulation can develop leading to defective haemostasis with depletion of clotting factors and release of large amounts of fibrin degradation products into the circulation.

A low-grade process of intravascular coagulation also occurs in pre-eclampsia. The disturbance of the balance between clotting and fibrinolysis in pre-eclampsia seems to be localized to certain areas of the vascular tree, particularly the uterus and kidney. Thrombotic occlusion appears to contribute to the impairment of placental blood flow and the development of placental infarction and ischaemia which occur in pre-eclampsia and in pregnancies complicated by impaired fetal growth. In pregnancies complicated by severe placental insufficiency treatment with heparin and dipyridamole improved placental function and fetal growth.

Further knowledge of the physiology and pathology of the coagulation and fibrinolytic systems may open up a new field of rational treatment for several of the hazards inherent in pregnancy.

Mycoplasmas and Human Infertility?

J. DE LOUVIS, M. BLADES, R. HARRISON,

ROSALINDE HURLEY, AND VALERIE STANLEY (*Queen Charlotte's Maternity Hospital, London*) There have been reports that eradication of T-strain mycoplasmas by appropriate antibiotics has been followed by pregnancy in couples adjudged infertile. The authors are engaged in studies of the incidence of *Mycoplasma hominis* and T-mycoplasmas in infertile and fertile couples, preliminary to a double-blind controlled trial of doxycycline in the treatment of infertility of unascertained cause. One hundred and twenty infertile couples and 36 fertile couples are the subjects of the studies so far conducted.

The criteria of infertility, and the materials and methods used, the sites sampled, and the incidence of *M. hominis* and T-strain mycoplasmas will be reported.

A Case of Carcinosarcoma of Ureter

H. B. MCDADE, E. M. ARMSTRONG, AND A. J. GRAHAM, (*Departments of Pathology and Urology, Western Infirmary, Glasgow*) Carcinosarcoma of ureter is an extremely rare neoplasm of which only one previous case has been described in the literature. The patient in the present case is a 60-year-old retired general labourer who presented in December 1971 complaining of haematuria and some colicky abdominal pain. Repeated cystoscopic examinations showed no significant pathology until January 1973 when a necrotic friable tumour mass was seen exuding from the R ureter. A R uretero-nephrectomy was performed in February 1973 and showed that the tumour was arising at the junction of the middle and lower thirds of the ureter and extended as a 1 cm diameter stalk of material down to the ureteric orifice. Histological examination revealed an intimate admixture throughout the tumour of both malignant epithelial and malignant stromal elements. After an initially good postoperative recovery the patient presented again in May 1973 with a recurrence of symptoms and examination revealed a recurrence of tumour in the region of the R ureteric orifice. This was removed and the site thoroughly treated with diathermy. The patient has remained symptom free and in good health since then with no cystoscopic evidence of recurrence. The diagnostic difficulties and pathogenesis of this neoplasm will be discussed.

Immunological Aspects of Hepatobiliary Disease

A. MILFORD WARD, G. ELLIS, AND D.

GOLDBERG (*Hallamshire Hospital Medical School, Sheffield*) Immunological and immunochemical parameters are useful adjuncts to the more usual liver function tests in the diagnosis and management of hepatobiliary disease. The profile, as it has been developed, consists of a series of tests which are technically easy to perform.

Serum immunoglobulin levels in liver disease are of particular value in distinguishing between the inflammatory and the essentially surgical hepatic lesions. Recognizable patterns of immunoglobulin profile may be discerned. This pattern recognition is improved by the consideration of the non-organ specific antitissue antibodies to nuclei, mitochondria, and smooth muscle. The detection of α_1 fetoprotein by a purely qualitative procedure assists in the diagnosis of increased hepatocyte turnover. The α_1 antitrypsin level is determined in selected cases, mainly paediatric, to exclude the intrahepatic cholestasis and progressive cirrhosis of antitrypsin deficiency. The profile is completed by screening for HAA and its attendant antibody.

The immunochemical determination of albumin has been added to the profile. This was done because the immunochemical albumin represents a truer picture of the serum albumin than the more conventional methods in those cases where the level is abnormally low, or where an elevated bilirubin interferes with its determination.

Pattern recognition with this profile may be summarized with reference to seven main conditions or groups of conditions:

Acute hepatitis

IgM elevation 300-1000 mg/100 ml (345-115 000 IU/ml) in 70% and antibody to smooth muscle in 60%. In the late stages of the disease IgG elevation become more prominent, and weak positive reactions for α_1 fetoprotein are seen with hepatocyte regeneration.

Chronic hepatitis

IgG and IgM elevations in 80%, antibodies to nuclei in 45%, and to smooth muscle in 54%. This group may be subdivided into chronic aggressive hepatitis in which IgG elevation and antibodies to nuclei predominate, and chronic persistent hepatitis in which IgG and IgM elevation and antibodies to smooth muscle predominate.

Primary biliary cirrhosis

IgM elevation 350-1500 mg/100 ml

(400-172 500 IU/ml) in 100% and antibody to mitochondria in 85%. Moderate elevations of IgG were seen in 60%.

Micronodular cirrhosis

IgA elevations in excess of 600 mg/100 ml (350 IU/ml) were seen in 70%.

Cholecystitis

Immunoglobulins and antibodies usually normal although four/eight cases of cholangitis showed elevation of IgM with attendant mitochondrial antibodies.

Extrahepatic obstruction

Immunoglobulins normal except for a variable mild IgA elevation. Antibodies uniformly negative.

Intrahepatic cholestasis

Immunoglobulins and antibodies normal save for two individuals who had IgM elevations and antibodies to nuclei.

Histological Aspects of Jaundice

P. J. SCHEUER (*Department of Histopathology, Royal Free Hospital, London*) Histological examination of liver biopsies helps to distinguish between different causes of jaundice. Haemolysis leads to iron deposition in the liver. In Gilbert's disease, a common form of non-haemolytic hyperbilirubinaemia, the liver is histologically normal, whereas in the Dubin-Johnson type of conjugated hyperbilirubinaemia the liver cells contain abundant iron-negative pigment.

The above conditions are distinct from cholestasis, in which bile as a whole fails to reach the duodenum in normal quantities, either because of mechanical obstruction or as a result of intrahepatic disease. From the histological point of view, cholestasis is the presence of demonstrable bile in tissue sections.

In acute cholestatic jaundice the practical problem in liver biopsies is usually the differentiation of acute hepatitis of viral type, drug-induced cholestasis such as that produced by chlorpromazine, and mechanical obstruction to large bile ducts. Other possibilities include hepatitis due to other causes such as drugs, alcohol, or infective agents, and chronic liver disease presenting acutely. In viral hepatitis the diagnostic lesion is the widespread and pleomorphic alteration of liver cells, accompanied by inflammatory-cell infiltration. Portal lesions are present but are less specific. Some drugs may produce an identical picture. Drug-

induced cholestasis is accompanied by little inflammation, and may be very difficult to distinguish from other forms of cholestasis without inflammation, such as idiopathic recurrent cholestasis and cases of mechanical biliary obstruction in which typical portal changes have failed to develop. These changes include oedema and acute inflammation of the tracts and proliferation of bile ducts.

Of the many forms of chronic cholestasis, primary biliary cirrhosis may be more common than previously supposed. Needle biopsies may not contain the classical bile duct lesions and granulomas, but may show characteristic changes, notably lymphoid aggregates.

Bilirubin Conjugation and Excretion

BARBARA H. BILLING (*Department of Medicine, Royal Free Hospital, London*) Bilirubin can only be excreted in the bile (or urine) if it is first converted into a polar derivative. This is mainly achieved by the formation of mono and di-glucuronide esters although recent studies have indicated that conjugation with glycosides and acidic disaccharides may also be important, particularly in obstructive jaundice. The microsomal enzyme responsible for the conjugation of bilirubin, bilirubin UDP glucuronyl transferase, appears to be the rate-limiting factor in the transfer of bilirubin from the plasma into the bile. A deficiency of the enzyme will therefore reduce the rate of clearance of bilirubin from the plasma and cause an unconjugated hyperbilirubinaemia, such as is commonly seen in the newborn. In the adult an absolute deficiency of the enzyme is extremely rare (Crigler Najjar syndrome) but a relative deficiency is not uncommon and has been found in all patients with Gilbert's syndrome. This benign condition is characterized by a mild unconjugated hyperbilirubinaemia (0.8-5.0 mg/100 ml) in the absence of overt haemolysis or coexistent hepatic or systemic disease. The incidence of Gilbert's syndrome in the general population is uncertain but values of the order of 0.5% for males and 0.15% for females have been cited. The degree of hyperbilirubinaemia tends to fluctuate and can be reduced by the administration of drugs such as phenobarbitone and glutethimide and raised by fasting and infection.

The capacity of the liver to conjugate and thus to excrete bilirubin is rarely exceeded except after a severe haemolytic episode or following the administration of