Twenty-eight isolates of *Enterobacteriaceae* were obtained from inpatients and outpatients with significant urinary tract infections. The effect of co-trimoxazole or its separate components was then determined upon shake cultures of these organisms in urine obtained from healthy subjects. Co-trimoxazole did not have a significant bactericidal effect upon any of the organisms. Trimethoprim alone had a bactericidal effect upon about one quarter of the organisms. Sulphamethoxazole thus appears to antagonize the bactericidal effect of trimethoprim in urine.

Volunteers were given therapeutic doses of either co-trimoxazole or equivalent amounts of its individual components. Urine from these individuals was found to have a similar effect upon the test organisms as synthetic mixtures of these various antimicrobials in normal urine.

There appears therefore to be a good case for further clinical trials to compare trimethoprim and co-trimoxazole in the treatment of urinary tract infections.

Benign Tumours of the Kidney in Infancy

A. H. CAMERON (*The Children's Hospital, Birmingham*) The salient features of six apparently benign tumours of the kidney are present. All occurred in infancy and were detected by abdominal palpation. All were large and one was initially considered to be an inoperable nephroblastoma. Some were solid and some were cystic. The histological appearances vary. Some have a well differentiated fibromatous pattern and others consist of simple cysts lined by inactive epithelium. More cellular areas are seen and dysplastic features may be encountered. The literature is briefly reviewed with particular reference to the confusing terminology in current use. The relationship of these tumours to renal dysplasia and nephroblastoma is briefly discussed.

References

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The Effect of Vitamin C on the Blood Vessels

CONSTANCE R. SPITTLE (*Pinderfields General Hospital, Wakefield*) Following a chance observation that I could reduce my serum cholesterol with vitamin C, a study was done on other healthy people, and a group

of patients who had had a coronary thrombosis. It was found that while the serum cholesterol of young healthy people went down after vitamin C, in patients with coronary artery disease it tended to rise. This was attributed to mobilization of arterial cholesterol, and previous experimental evidence supported this. Vitamin C acts on the other fat fractions also: the lipoproteins, lipoprotein lipase activity, and the triglycerides. It also provides the ground substance for the arterial walls. Thus, a balance exists between vitamin C and fat. If the balance permanently favours vitamin C, the cholesterol will always be delivered to the liver, the β -lipoproteins will remain low, the lipoprotein lipase activity will be high, so the triglycerides will be low, and the arteries will be well supplied with ground substance, so they will remain clean. If the balance favours the fats, there will be a gradual accumulation of cholesterol in the arteries, the other fat fractions will gradually become abnormal, and the arteries will lose their ground substance, so atherosclerosis will result.

Direct proof of this hypothesis is impossible, but it is possible to show the powerful protective action of vitamin C against thrombosis in the veins. The results of a double-blind study are shown. Clinical deep vein thrombosis has now disappeared from our surgical wards.

Investigation of Cutaneous Inflammatory Response in Polycythaemia Vera

M. L. GHOSH, G. HUDSON, AND E. K. BLACKBURN (*Department of Haematology, University of Sheffield*) Changes in the inflammatory response to a simple skin abrasion, made under aseptic conditions, may be of value in studying haematological disorders such as malignant lymphoma (Ghosh, Hudson, and Blackburn, *Brit. J. Haemat.*, **25**, 293, 1973). In the present investigation, patients with established polycythaemia rubra vera, together with control subjects, have been studied by this technique.

The number of cells present in the exudate at 48 hr was a prominent feature in untreated polycythaemia. As compared with the control (10%), there was a significantly higher percentage of granulocytes (23%) and a correspondingly reduced percentage of macrophages. In the peripheral blood of these patients, the total white cell and neutrophil counts were significantly higher than in normal controls. Statistical analysis showed that

there was a relationship between the blood and skin window cell counts in respect of both neutrophils and eosinophils. In polycythaemic patients in remission, the skin window results were generally similar to the controls except in that basophils were increased.

The results provide no evidence of a quantitative defect in the cutaneous inflammatory reaction in polycythaemia vera, but suggest that the mechanisms underlying the basophilia may be worth investigating further.

The Influence of Oral Contraceptives on the Ratio of Factor VIII Activity to Factor VIII Related Protein

PENELOPE STABLEFORTH, MARGARET A. HOWARD, DANIELLE C. MONTGOMERY, MARY REAVLEY, ELAINE WILSON, WENDY L. CHURCHILL, KATHERINE M. DORMANDY, AND R. M. HARDISTY (*Hospital for Sick Children, London, and Royal Free Hospital, London*) Determination of the ratio of factor VIII activity to factor VIII related antigen (factor VIII RA) has proven to be a useful means of detecting carriers of haemophilia A.

Bouma *et al*¹ and Van Royen *et al*² have shown that during the last trimester of pregnancy the ratio of VIII activity to VIII RA is lowered due to an excessive increase in the level of VIII RA.

Oral contraceptives, like pregnancy, cause an increase in VIII activity but as the effect of oral contraceptives on VIII RA levels was not known, the present investigation was initiated between the Hospital for Sick Children and the Royal Free Hospital, London.

Twenty-four normal women taking oral contraceptives, age matched with normal women not taking the 'pill', were bled on three occasions at seven-day intervals.

The PT, PTT, and factor VIII activity were measured on fresh blood, and the VIII RA was measured by the Laurell technique using two different rabbit antibodies.

Early results indicate no appreciable difference between these two groups.

This suggests that, unlike pregnancy, oral contraceptives do not alter the ratio of VIII activity to VIII RA making it possible to diagnose haemophilia carriers taking oral contraceptives.

References

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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. 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 65-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.