incorporation of radioactive precursors, is unimpaired, we investigated protein synthesis using labelled leucine. A proportion of cells throughout the cell cycle showed no evidence of uptake.

It is postulated that this may be due, not to the failure of DNA synthesis, but to a separate defect resulting from inability of B_{12} coenzymes to methylate both transfer and messenger RNA, and that RNA, although synthesized, is ineffective until methylation occurs. Such an action has not been described in man although there is biochemical evidence to support it.

INHIBITION OF FACTOR XIII BY HEPARIN

J. GREEN (Perth) In human citrated plasma clotted by thrombin, comparison, at equivalent clotting times, of the weight of fibrin formed and the fraction soluble in 6 M urea shows that in the presence of heparin, the total weight of fibrin formed is less, and the rate and the extent of cross-linkage, as measured by the weight of urea-insoluble fibrin, is decreased. There is some variation between plasmas, but all samples studied at pH 7.0 with minimal dilution have shown complete inhibition of cross-linkage at heparin levels of 8 units/ml and clotting times longer than 30 seconds. Dilution of plasma at constant ionic strength results in cross linkage occurring at lower thrombin/heparin ratios.

The inhibitory effect of heparin can be reversed by protamine sulphate after clotting has occurred.

In fibrinogen preparations of increasing purity, inhibition of cross-linkage by heparin is increasingly difficult to demonstrate, suggesting that other factors may be involved.

THE POSSIBLE PHYSIOLOGICAL SIGNIFICANCE OF THE MICROANGIOPATHIC RED CELL FORM

C. WARDROP AND H. E. HUTCHISON (Glasgow) Irregularly-contracted erythrocytes (burr cells) are a recognized sign of red cell damage, often associated with vascular disease, and this may sometimes lead to a frank haemolytic state—the microangiopathic haemolytic anaemia syndrome.

Recent experimental work by Dacie *et al* (Bull, Rubenberg, Dacie, and Brain, 1967; Rubenberg, Bull, Regoecki, Dacie, and Brain, 1967, has provided further information on the pathogenesis of such haemolysis and cases consistent with their suggestions are described.

Other clinical associations of irregularly-contracted red cells exist which the Dacie hypothesis would not readily explain. Some of these associations and their possible pathogenesis are discussed in the light of current concepts of the fibrinolytic system.

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RENAL BIOPSY: AN ASSESSMENT OF ROUTINE ELECTRON MICROSCOPY

J. R. TIGHE, A. E. CLARK, A. J. EISINGER, AND N. F. JONES

(St. Thomas' Hospital, London) Renal biopsies have been routinely examined by electron microscopy during the past two years. Of 103 biopsies, 83 from 79 patients were suitable for this study. Dissecting microscope examination enabled the adequacy of the biopsy to be assessed and suitable pieces selected for electron microscopy. The whole biopsy was also examined by light microscopy. Processing for electron microscopy takes four days.

The investigation proved to be of most value in cases of the nephrotic syndrome. Of eight patients diagnosed on light microscopy as minimal change glomerulonephritis, three were subsequently reclassified on electron microscopy as membranous glomerulonephritis. Of these, two failed to respond to steroid therapy. In contrast, four of the remaining five patients with minimal change glomerulonephritis responded to treatment with steroids and the fifth has not been followed long enough to assess response. Only one of 11 patients with membranous glomerulonephritis is known to have had a complete remission with treatment. In patients with less severe proteinuria electron microscopy revealed abnormalities, such as foot process disease, which were not apparent in the light microscope.

Electron microscopy is of much value in the diagnosis of minimal deposits of amyloid when the results of light microscopy are equivocal.

The characteristic basement membrane deposits of streptococcal proliferative glomerulonephritis are confirmed.

Routine electron microscopy of renal biopsies, particularly in the nephrotic syndrome, is desirable, but because of the considerable cost, these facilities may well have to be based on regional centres.

HEPATIC AND RENAL DAMAGE WITH PARACETAMOL OVERDOSAGE

R. A. G. BROWN (Dundee) N acetyl para amino phenol was discovered in 1889, recognized as a metabolite of phenacetin with good analgesic properties in 1949, and introduced into British clinical medicine in 1956.

Since then reported toxic effects have been few and the sales of various paracetamol-containing compounds have increased to an estimated 680 million in 1967.

During 1967, five patients admitted to Dundee Royal Infirmary were cases of paracetamol self poisoning. In three, there was histological evidence of hepatic damage, varying from centrilobular fatty change and cloudy swelling to frank centrilobular necrosis, along with an increase in lipofuscin pigmentation and increased mitotic activity signifying regeneration. The remaining two showed clinical evidence of hepatic derangement. In one, a fatal case, there was renal damage. The capsular spaces contained a foamy lace-like material—presumably proteinous—which spilt over into the proximal convoluted tubules and there was evidence of distal tubular degeneration with focal necrosis. The renal papillae appeared intact.

Paracetamol, reputedly the analgesic of choice for occasional use, is freely available, but in overdosage it is potentially lethal.