assess the validity of a two component hypothesis in man.

Healthy, non-atopic, male subjects (n = 5) were given intradermal injections (50 ul per site) of coded solutions which were assigned randomly toirced sites on the forearm. Two perpendicular diameters and the thickness of the resulting wheals, as well as the diameters of erythema, were measured 12 min later. Wheal volumes, and areas of erythema, were calculated and have been presented as (mean ± s.e. mean).

Combination of prostaglandin E2 (PGE2, 0.5 ug) and bradykinin (Bk, 1 ug) resulted in a significantly greater (p < 0.005; paired t-test) wheal volume (175 ± 20 ul) than could be accounted for by summation of the responses to Bk (53 ± 16 ul) and PGE2 (34 ± 11 ul). Histamine (H, 0.1 ug) produced a wheal response which was not potentiated by PGE2 (H: 51 ± 8 ul; PGE2: 26 ± 9 ul; H + PGE2; 53 ± 11 ul). The response to H + PGE2 was significantly less (p < 0.025) than expected from summation of responses to the individual components. H, but not Bk, produced erythema (8.8 ± 1.4 sq cm) in all subjects.

The synergistic interaction observed, in man, between Bk and PGE2 in the production of cutaneous wheal responses is consistent with the two component hypothesis of acute inflammation established in experimental animals. However, the lack of synergism between H and PGE2 is at variance with animal data.

69 ENHANCED PRODUCTION OF PROSTAGLANDINS BY SYNOVIAL CELLS IN THE PRESENCE OF POLY (I-C)

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We have been investigating interactions between cells present in the inflamed joint using cultures of human tissue and cells.

Medium conditioned by cultured peripheral blood mononuclear cells (MCF) can stimulate synthesis of prostaglandins and produce PGE and proteases such as collagenase and plasminogen activator, which may be involved in the inflammation and connective tissue breakdown observed in rheumatoid arthritis. Yaron et al. have shown that human synovial fibroblasts can be stimulated by interferon and poly (I-C) to produce increased amounts of PGE.

We have found that poly (I-C) stimulates the production of PGE by our enzyme-dispersed synovial cell cultures, thus confirming the above observations. Furthermore, poly (I-C) also stimulates the production of plasminogen activator by synovial cells. The time courses of response to MCF and poly (I-C) are very similar, first detectable within 2 hours and maximal after 12 hours. The effects of both are inhibited by dexamethasone, and are sensitive to protein synthesis inhibitors.

The relationship between MCF and the interferon system will be discussed. The effects of interferon in terms of anti-viral and anti-tumour cell activity have been widely publicised, but it may be that its primary function is to serve as an intracellular messenger. Interactions between immunological cells are complex, and it could be that overproduction of interferon, e.g. as the result of a primary lesion in the immune system, is involved in some of the deleterious effects observed in diseases such as rheumatoid arthritis.


70 ALTERATIONS IN GLUCOCORTICOIDS AND THYROID HORMONES IN ANOREXIA NERVOSA


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Alterations in the peripheral metabolism of thyroxine (T4) are well known in states of reduced calorie intake. Both reduced levels of thiol co-factor and the activity of 5'-deiodinase have been implicated in the reduction of 3,5,3'-triiodothyronine (T3) production. How these changes are mediated are uncertain, although increased glucocorticoid has been shown to induce similar changes in humans and experimental animals. To investigate further any role of glucocorticoid in these changes, total serum cortisol (TSC), cortisol binding globulin (CBG), urinary free cortisol (UFC), together with serum T4, T3, and 3,3',5'-triodothyronine (tT3) were measured in anorectic patients taking a supervised diet to regain weight. CBG was assayed using a monospecific antiserum produced in a similar fashion to that previously described for thyroxine-binding globulin (Bradwell et al., Clin Chim Acta 71, 501, 1976). As the patients (n=42) regained weight there was a tendency for TSC to fall (p < 0.001) and CBG to rise (p < 0.001), whilst serum T3 increased (p < 0.001) and tT3 fell (p < 0.001). Serum T4 was largely unchanged. The ratio of TSC:CBG, which may be regarded as an index of unbound cortisol in serum, was also reduced as weight was regained (p < 0.001) and a similar reduction was seen in UFC although this was less clear cut. These results demonstrate that changes in the availability of serum cortisol to peripheral tissues parallel changes in the circulating levels of T3 and tT3 in these patients, although by themselves do not establish a causal relationship. Further they indicate that previously proposed changes in the affinity of CBG for cortisol are unnecessary to explain alterations in available cortisol in anorexia nervosa (Casper et al, J Clin. End. Metab. 49, 406, 1979).

71 HLA-DR ASSOCIATION WITH TYPE I DIABETES

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We have investigated DR antigens in 170 Type 1 (insulin dependent) and 29 Type 11 insulin