11. MONOCYTE FUNCTION IN RHEUMATOID ARTHRITIS (RA) WITH VASCULITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): EVIDENCE FOR A DEFECT IN IMMUNE PHAGOCYTOSIS

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Evidence is accumulating which suggests that cells of the monocyte/macrophage system may play a key role in the pathogenesis of RA. As part of a series of investigations of monocyte function in patients with rheumatic diseases a method has been developed for studying monocyte phagocytosis in cells separated from 10 ml of venous blood. Pre-opsonized heat-killed Candida albicans are mixed in suspension in Teflon wells and numbers of the extracellular yeast remaining are counted at timed intervals. Kinetic studies show that the rate of phagocytosis is first order with respect to both yeast and monocyte concentrations so that the efficiency of phagocytosis can be expressed by a rate constant.

Fourteen patients with definite or classical RA and 14 healthy volunteers matched for age and sex have been compared. The phagocytic rate constant was not different in patients with rheumatoid factor (RF)-positive RA compared with controls but was significantly reduced in all five RA patients with active vasculitis. Depression of the phagocytic rate constant was not correlated with clinical disease activity, erythrocyte sedimentation rate, titres of RF or antinuclear factors.

To determine whether this phagocytic defect is specific for either the Fe or C1 receptor on monocytes, the phagocytic rate constant for both IgG-coated C. albicans and C1-coated Saccharomyces cerevisiae has been measured in patients with rheumatoid vasculitis and SLE. Preliminary results suggest that there may be a selective C1 receptor defect in rheumatoid vasculitis, and in SLE the Fe receptor or both may be involved. Results of parallel measurements of total complement activity (CH50), complement components (C3, C4, C5) breakdown products and C1Q binding will be presented.

13. CHARACTERIZATION OF THE HEPATOCYTE PLASMA MEMBRANE TRANSPORT MECHANISM FOR LACTATE

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Preliminary evidence has been presented for a stereoselective transport mechanism for lactate in hepatocyte plasma membranes (Monson et al., 1979, Clinical Science, 57, 30P–31P). The present work extends the findings by examining the kinetics of initial lactate uptake into isolated rat hepatocytes and the effects of potential inhibitors of anion transport, changes in extracellular pH and change in temperature on initial uptake. The cellular uptake of L(+)-lactate in 15 s involves two components; one is saturable but the other fails to saturate with extracellular lactate concentrations up to 30 mmol/l, suggesting passive diffusion as its likely basis. The passive diffusion component may be largely an artifact of the isolated cell preparation in which an abnormally large surface area is presented for diffusion. The saturable component, which is stereoselective, conforms to Michaelis–Menten kinetics, yielding values for V_max of 8.3 μmol min⁻¹ g⁻¹ wet wt. Lactate entry is not rate-limiting for overall lactate removal under these conditions but could be in vivo under some circumstances.

Initial entry of lactate on the transporter is inhibited by d-cyano-3-hydroxycinnamate and by the thiol reagent p-chloromercuriphenylsulphonate, but not by the inhibitor of the general anion transporter 4-acetamido-4-isothiocyanostilbene 2,2'-disulphonic acid (SITS).

Lactate entry exhibits a high temperature dependence up to 25°C but apparent activation energy falls at higher temperatures in keeping with the behaviour of several anion-transport mechanisms.

Initial rate of entry is enhanced by lowering extracellular pH but the relationship of the lactate distribution ratio to that of H⁺ indicates that facilitated non-ionic entry is not the sole mechanism of "carrier"-assisted transport. This finding could be explained by either a hydrogen ion symport or hydroxyl ion antiport mechanism with additional exchange of lactate for another