environment of the hæm group has been affected, suggests that histidine residues are involved[6,7]. Experiments in progress using nitrophenylacetate, the hydrolysis of which is catalysed by imidazole[8,9], indicate that imidazole residues are made unavailable when $HgCl_2$ is added to metHb. The rate of hydrolysis of the ester by metHb is 1·5–2 times more rapid in the absence of $HgCl_2$ than in the presence of it ($HgCl_2$/protein = 6/1). As a result, at the present time, it seems that $HgCl_2$ is capable of reacting not only with the sulphydryl groups but also the imidazole residues of hæmoglobin.

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PATHOLOGY

Effect of RNA on Vascular Permeability in the Rat

Previous workers have shown that certain nucleosides and nucleotides can increase vascular permeability and cause leucocyte emigration[1–4] and thereby directed attention to their potential role as mediators of inflammation.

An extract has recently been prepared from lymph node cells (LNPF) which causes an intense increase in vascular permeability and immediate and prolonged emigration of leucocytes and the deposition of a material resembling connective tissue fibrinoid[5]. Immediately following the injection of LNPF the inoculum reacts positively for RNA with the Unna–Pappenheim stain. After 20 min, however, the positive RNA reaction can no longer be obtained.

Because of these findings it was decided to investigate the ability of RNA and also DNA to reproduce the effects of lymph node extracts. Highly polymerized DNA from calf thymus (B.D.H.) failed to increase vascular permeability in the rat in doses of 15 μg to 5 mg/ml. On the other hand, a purified preparation of highly polymerized yeast RNA (B.D.H.)[6] was active in increasing vascular permeability over the range of 15 μg–1 mg/ml. This preparation of RNA also induced extensive emigration of leucocytes within 15 min of injection, 100 μg leading to the accumulation of about 50 leucocytes per high power field. By 24 h after an injection of 100 μg of RNA, large numbers of mononuclear leucocytes were infiltrating the inoculation site. Unlike LNPF, however, injections of RNA did not lead to the accumulation of an eosinophilic coagulum at the site of injection. The effect of RNA on vascular permeability could not be destroyed by prior incubation with 1·5 mg/ml. ribonuclease (Sigma 50 units/mg) at 37° C for 1 h.

Unlike nucleosides, the effects of which appear to be due to release of histamine[3,4], the increase in vascular permeability induced by RNA could not be abolished by systemic dosage with the antihistamine drug mepyramine maleate ('Anthisan' 1–2·5 mg/kg) or the 5-hydroxytryptamine antagonist '*BOL* 148'. However, incubation of RNA with guinea pig plasma led to a striking suppression of its effect on vascular permeability as did local administration of sodium salicylate 2·5 mg/ml.[7]. In its response to these antagonists RNA bore a close resemblance to LNPF[8].

Other forms of RNA were found at first not to share the activity of the highly polymerized preparation, thus freshly made solutions of soluble yeast RNA sodium salt (B.D.H.) and soluble yeast RNA Type III (Sigma Co.) both failed to increase vascular permeability significantly when tested in rats' skin. On the other hand, when these same solutions were allowed to stand at room temperature, Seitz filtered and tested in rat skin, there was a progressive increase in activity, until after 24 h their effects were as great as that of the highly polymerized preparation. The effect of the aged solutions could not be attributed to the appearance of histamine-releasing nucleosides[4] since dye leakage was not diminished by administration of mepyramine maleate (2·5 mg/kg). The true explanation of this phenomenon is not yet apparent.

Nevertheless the results so far are consistent with the view that RNA or a derivative, for example, an oligonucleoside, might be responsible for some of the phlogistic effects of extracts of lymph nodes and perhaps other tissues.

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Early Regressive Changes during the Tuberculin Skin Reaction

For an understanding of the pathogenesis of pathological processes, the initial stages of their development are usually most important. At first only the direct sequelæ of the causal agent play a part, and the position is not very complicated by regulatory and reparative processes aiming at the renewal of the normal state. The morphology of early stages of the hypersensitivity reaction of the delayed type has been examined by several authors[1–4], who directed attention mainly to the composition of the cell infiltrate. Because inflammatory infiltration is a result of tissue damage, I was interested rather in changes in tissues where the immunological reaction takes place.

I used white guinea pigs weighing 250–350 g, sensitized by injection of 0·1 ml. emulsion into both hind limbs of the following composition: 6 ml. paraffin oil, 2 ml. lanolin, 3 ml. physiological saline containing per 1 ml. 3 mg BCG vaccine killed by heat (1 h at 70° C). The skin tests were carried out 21–28 days after sensitization with 10, 1 and 0·1 μg PPD (Statens Scruminstitut, Copenhagen, Denmark) in 0·1 ml. physiological saline into the skin of the hip. The groups formed by five sensitized and one control guinea pig were killed 1/2, 1, 2, 3, 6, 12 and 24 h following the skin test. The sites of the skin test were examined in