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"COMPARATIVE PATHOLOGY OF INFLAMMATION IN THE SHEEP"

A thesis  
presented in partial fulfilment of the requirements  
for  
the degree of Doctor of Philosophy  
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1967

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## Summary

- (1) The inflammatory response in the sheep has been investigated using experimental methods developed in similar work on laboratory animals.
- (2) A biphasic increase in vascular permeability occurs following turpentine and thermal injury; an early phase seems to be mediated by histamine. In contrast, mediation of the delayed phase, which appears to be the major part of the response, remains uncertain. Histamine, a "Globulin Permeability Factor" and possibly kinins, probably participate. 5-Hydroxytryptamine does not appear to be a natural mediator of inflammatory reaction in the sheep.
- (3) Histamine is readily released in sheep skin, and in response to a wide variety of stimuli.
- (4) The occurrence of the delayed phase does not depend on the operation of the histamine - mediated early phase.
- (5) Strophanthin-G, which interferes with ionic transport across cell membranes, suppresses the early histamine phase of inflammation in the sheep.
- (6) Cutaneous antigen-antibody reaction of the Arthus-type has been found to be associated with histamine release in the sheep.

- (7) The effects of sodium salicylate, cortisone and indomethacin on the permeability response in the sheep are recorded. In all cases, a significant suppression of exudate formation was obtained in the delayed phase of the permeability response following intrapleural injection of turpentine. These effects differ from those reported in the rat.
- (8) A factor which increases vascular permeability both by the release of histamine and apparently through another mechanism, has been isolated from lymph node cells of normal sheep. This is termed "lymph-node-permeability factor".
- (9) Most of the increase in vascular permeability in the inflammatory reaction in the sheep is associated with venules and comparatively little with capillaries.
- (10) Increased vascular permeability and emigration of leucocytes from blood vessels are dissociated phenomena.
- (11) Permeability substances activated or released by injury do not appear to exert much effect on the emigration of leucocytes.
- (12) Mast cells appeared locally more numerous in the sheep skin following turpentine injury and the injection of various permeability-increasing substances.

- (13) Histamine in doses of 100 µg attracted eosinophiles to the site of injection in the sheep skin.
- (14) Total denervation did not affect the permeability response in inflammatory reaction to turpentine injury in sheep skin.
- (15) Toxic doses of compound 48/80 and of histamine produced sudden death in sheep. The post-mortem picture has been compared to that seen in clostridial infections in sheep, and the suggestion is made in these infections release of histamine in large or even toxic amounts may contribute to the cause of death.
- (16) The results obtained in the sheep suggest a closer similarity between that animal and the guinea-pig than between sheep and rat. Certain features are common to all.
- (17) The present work has revealed that there are clear differences between species in the inflammatory mechanism. While information obtained in one species may provide some information for another, inter-species differences may be wide and basic, and it is not possible to extrapolate results between species. Extensive work is required to categorise the mechanisms in domestic animals. This would provide a better understanding of the pathogenesis and pathology of diseases in them. It is felt that sheep may prove a useful animal in exploring certain basic problems of the inflammatory reaction.

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