funding science, the paths to application and exploitation—and with the professionalisation of science and discipline differentiation within the sciences.

The history of science has come a long way from mere 'signpost' history, from Whiggish interpretations of past science which have served to justify the orthodoxy of the present, and from an insularity to the social and political context of the sciences. The initiative of the New York Academy of Sciences in bringing scientists together and including some historians is to be welcomed, not only as a means of adding to the sources for the history of science but in promoting personal contact between scientists and historians. □

Malaria, piroplasmosis and endotoxin

from F. E. G. Cox

ONE of the most unexpected observations to emerge from the massive amount of work directed towards an understanding of immunity to intraerythrocytic protozoa is that previous exposure to BCG or *Corynebacterium parvum* protects certain strains of mice completely against *Babesia* spp. and partially against *Plasmodium* spp. (see Cox *Nature* **273,** 623; 1978). BCG and *C. parvum* also sensitise mice to endotoxin and elicit a protective response against certain tumours (Snider *et al J. natn. Cancer Inst.* **60,** 785; 1978, Milas & Scott *Adv. Cancer Res.* **26,** 257; 1978). The implication has been that these agents or their products in some way cause macrophages, after stimulation by endotoxin, to release a soluble product that is instrumental in the destruction of rapidly dividing tumour cells (Carswell *et al. Proc. natn. Acad. Sci. U.S.A.* **72,** 3666; 1975). The release of such a substance is also brought about by the yeast cell wall polysaccharide, zymosan, and the discovery that zymosan also protects mice against *Babesia* spp. and *Plasmodium* spp. has led I. A. Clark of Canberra to put forward a new hypothesis linking sensitisation to endotoxin with the intraerythrocytic death of blood parasites and the pathogenesis of malaria and piroplasmosis (*Lancet* **ii,** 75; 1978).

Clark has shown that during the course of infections with *Babesia microti* in CBA mice the animals become increasingly sensitive to endotoxin in the form of bacterial lipopolysaccharide (LPS) being several hundred times more sensitive at the peak of the infection than at the beginning or end. Similar results were obtained with *B. rodhaini* and the malaria parasites *Plasmodium vinkei petteri* and *P. berghei*. It seems reasonable, therefore, to assume that mice become sensitised to endotoxin during the course of the infection and at the peak, when presumably vast amounts of parasite material are being released, a phenomenon analogous to endotoxin challenge occurs. This causes macrophages to release soluble factors that kill the parasites within the red cells resulting in the crisis associated with resolving infections. The intracellular death that occurs at the crisis is seen both in naturally resolving infections and in mice pretreated with BCG or *C. parvum* and challenged with large numbers of parasites.

Endotoxin shock has been shown to produce many effects including polyclonal B lymphocyte stimulation and depression of T lymphocyte activity both of which are associated with the crisis in malaria infections. The pathology of malaria and piroplasmosis is similar and in malaria in particular it has long been thought to have much in common with endotoxin shock (Neva *New Engl. J. Med.* **277,** 1241; 1967). Thus all the events that occur during an infection could well be part of the same process.

If the death of the parasites is brought about as a result of endotoxin shock it might be expected that anything that sensitised mice to endotoxin would have the same effect and Clark has produced evidence to support this by showing that *Brucella* and *Coxiella* protect mice against intraerythrocytic protozoa as effectively as BCG and *C. parvum*.

This new hypothesis poses as many questions as it answers. It is not clear, for example, whether or not the parasites themselves produce endotoxin, for this has certainly not been easy to detect, but this may be because the quantities involved are so small. Alternatively, sensitisation may occur through the gut flora, for the permeability of the gut is known to be affected by blood parasites, or by antigen–antibody complexes (a theory that would be attractive to immunologists). The nature of the actual macrophage product is still obscure. It might be tumour necrosis factor (Carswell *et al. Proc. natn. Acad. Sci.* **72,** 3666; 1975) or it could even be arginase, which has recently been shown to be produced by zymosan and endotoxin-stimulated macrophages (Currie *Nature* **273,** 758; 1978). Arginase brings about arginine deprivation which presumably could adversely affect the rapidly dividing intraerythrocytic parasites. The problem is that we simply do not know enough about the biochemistry of either the parasites or the various macrophage products that might affect them.

The big question, however, is how relevant this is to human and veterinary medicine. Here Clark produces a mass of circumstantial evidence to suggest that his hypothesis is a general one. It remains to be seen whether or not the weight of contradictory evidence which will inevitably be produced outweighs this supporting evidence. There are some exciting times ahead in this new area which is one with which few parasite immunologists have so far become involved. □

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Hormone binding in plants

from C. J. Lamb

THE existence of plant growth regulators such as auxins and cytokinins has been known for some time and a plethora of physiological responses to each class of hormone have been described. However, little is known of the biochemical basis of plant hormone action. By analogy with animal hormones one might expect receptor proteins which bind the hormone and as a result of this interaction, initiate the biochemical reactions leading to the physiological response. Characterisation of such receptor proteins is of considerable interest since they are potential sites for the action of herbicides and synthetic growth regulators, and recently a number of workers have overcome considerable theoretical and technical difficulties to characterise hormone binding sites with the properties expected of plant hormone receptors.

There are no known receptor mutants in plants and the primary responses to hormones have not yet been elucidated. Therefore indirect methods are needed to assess the biological relevance of plant hormone binding. An excellent illustration of the attendant problems is provided by the work of Sussman and Kende[1] on cytokinin binding to a particulate fraction from cultured tobacco cells. Bound hormone can be separated from free hormone by sedimentation of the par-

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