SYMPOSIUM ON FACIAL ECZEMA RESEARCH

INTRODUCTION

C. P. McMEEKAN*

THIS SYMPOSIUM on research into the problem of facial eczema has been organized at the request of the programme committee of this Society. It was argued that the recent dramatic developments involving, not only a break through the curtain of mystery that has surrounded this problem for so long, but also the advent of highly powered and highly paid British reinforcements, warranted a day of this Society's time. In making the request the Committee emphasized that it appreciated that an attempt to cover the complete story of facial eczema was, perhaps, unjustified, and certainly impossible in the time allotted. It believed, however, that it would be worthwhile attempting a review of the key steps that had been responsible for the new knowledge. As the organizer of this symposium it is my function to introduce the subject and the speakers in such a way as to indicate to you most features of the story which I hope will be unfolded. Because of the restriction necessarily imposed by space, and the narrow compass of the assignment, I would emphasize that we are not pretending to cover all the manifold aspects of facial eczema. It is our purpose merely to tell the story, as accurately as possible, of the sequential chain of events that have helped us to the present stage where a fungus is considered responsible for producing the toxin of this disease.

I am not apologizing for the fact that the majority of speakers in this symposium are members of my staff. I would merely remind you, in justification, that for 15 years at least, this small band of workers has stood alone to suffer the slings and arrows of outrageous criticism. That today we are supported by so many research stations and so many scientists of such high calibre, is so much a matter of encouragement to us that we are not ashamed to exhibit the ignorance that for so long characterized our place in the scheme of things.

* Ruakura Animal Research Station, Dept. of Agriculture, Hamilton.

Six well defined and sequential steps have led us to the present position. The papers that are to follow will deal with these steps in detail. The steps were:

(1) Recognition of the key features of the pathology of the disease.

(2) The development of techniques for the collection of toxic grass.

(3) The discovery of a small animal assay for toxicity.

(4) Chemical fractionation and purification of the toxin and identification of an associated chemical.

(5) The development of the "beaker test" for toxicity.

(6) The incrimination of a specific fungus.

First the basic features of the pathology were recognized. Facial eczema was shown to be a liver disease characterized by severe occlusive damage to the bile duct system. Experimentally it was determined that the photosensitization responsible for skin lesions was a secondary symptom resulting from inability of the damaged liver to excrete the light-sensitive breakdown product of chlorophyll, phylloerythrin. The physical character of the liver damage and the failure of all attempts to transmit the disease from animal to animal led to the hypothesis that a specific toxin was responsible. Research thereafter was directed toward identification of the toxic factor involved.

Secondly, field observations and experiments showed that the liver damaging factor was contained in or on pasture grazed by affected stock. The sporadic occurrence of the disease in time and place, the transient character of the toxin and the delay between ingestion of toxic grass and the appearance of symptoms all had to be recognized and evaluated before suitable field techniques were devised for collecting and preserving toxic grass with which to work. The chemist could not be used until this step was taken. Progress was also delayed because of lack of a suitable small animal assay. Toxicity could be detected only by feeding suspect pasture to lambs which, by virtue of their size, were far too extravagant in their use of the limited amounts of toxic material available.

Thus, the third key step was the discovery that the baby guinea pig was susceptible to the toxin and a guinea pig assay was developed, based on a standard feeding procedure followed by liver examination.

The fourth step now became possible. For the first time and only after a 15-year wait, the chemist was provided with reasonable supplies of material of proven toxicity and a small animal assay with which to test chemical extracts and guide fractionation procedures. Rapid progress toward purification and identification of the toxin was made; the toxin theory was substantiated by production of the disease in the laboratory and the amount of the toxin in dried grass was shown to be but a few parts per million. In the process, a chemical substance was observed which, though not the toxin itself, appeared always associated with it.

This led to the fifth step, an indirect chemical test for toxicity. The chemical substance concerned was studied and a rapid method devised for detecting its presence in grass samples. The resultant so-called "beaker test", capable of being carried out on grass samples in a few hours compared with 35 days with the guinea pig, could be used as a pointer to toxic periods and toxic samples. Unexpectedly it provided the key to the last link in the chain.

The chemical substance of the "beaker test" was such that a fungal origin was indicated. Various other facets of information gathered along the way pointed in the same direction. That a fungus might be responsible for the disease had been postulated 20 years before, but early attempts to test such an hypothesis had failed and had been abandoned in favour of a theory of an aberrant plant metabolite. In a revival of effort, the systematic collection, culture and identification of a host of soil and surface microorganisms from a facial eczema hot-spot area and the testing of unusual types by guinea pig feeding was embarked upon. Results were negative. Eventually, however, the spores of *Sporidesmium*, collected from a gang mower after an eczema suspect period, proved positive to the "beaker test". This was the first scientific evidence of a possible fungus-facial eczema association. Quite quickly the organism was identified, grown in pure culture and the disease produced in the laboratory in both guinea pigs and lambs.

An important lesson from this story is that each step forward was dependent upon the step that had preceded it. Thus the mycologist of 1938 had no chance of incriminating any fungi as the techniques necessary to do so had not been discovered. The second lesson is a large number of scientific specialists, working as a team, who contributed to the six steps—veterinarians, histopathologists, biochemists, organic chemists, physiologists, microbiologists and agriculturalists were primarily involved. The third

point is one that cannot be too often stressed in any consideration of the organization of scientific endeavour. It was only by the co-operative efforts of such a diverse team, the members of which were not associated with any one station or any one government department, that the work has been carried to the present stage. In this connection, I personally, deeply appreciate the generous spirit of co-operation on the part of other research stations and personnel that has characterized my association with the investigation over the past 15 years.

In giving place now to the subsequent speakers I would like to express the hope that they will, in fact, achieve the objective of this Society in placing on record for all time the contributions of the many individual workers who have played a part, small or large, in the efforts so far. In particular may I, personally, pay a tribute to the leader of research in facial eczema, John Filmer. Although he has exasperated me sometimes beyond endurance, I would like to express my admiration of his single minded line of attack on the problem—an attack which has yielded handsome dividends.