

## ELECTIVE LOCALIZATION OF STREPTOCOCCI.

LECTURE BY DR. E. C. ROSENOW.

A POST-GRADUATE lecture was delivered on May 26th at the Royal Dental Hospital of London by Dr. E. C. Rosenow of the Mayo Clinic, Rochester, U.S.A., who reported the results of certain experiments which he had undertaken. The devitalized teeth of dogs were inoculated with streptococci derived from various infective lesions elsewhere in the bodies of human patients; similar lesions were reproduced in many of the dogs. The following abstract has been contributed by Dr. Rosenow.

If the streptococci shown to possess elective localizing power on isolation in a considerable number of diseases (as shown in a series of published reports) really have etiological significance in the different diseases studied, then they should localize and produce lesions in the specific organ or tissues, following other methods of inoculation. Owing chiefly to their relatively low virulence, this has been demonstrable in particular instances in different diseases following intraperitoneal, subcutaneous, intratracheal, intratibial, and intraocular infections, and, in diseases of the nervous system, after the intracerebral injection of suitable doses of cultures or of the material obtained directly from foci.

In order to remove all doubt that streptococci showing elective localizing power may produce disease in remote parts of the body through chronic, low-grade, symptomless foci of infection, such as occur commonly in human beings, we have inoculated the teeth of dogs with streptococci shown to possess elective localizing powers. Under ether anaesthesia the four cuspids were isolated, sterilized with tincture of iodine, and severed with a bone-cutting forceps. The pulps were removed and, under sterile conditions, the pulp chambers of three were inoculated with the cultures of the streptococcus in question. The opening was then sealed with gutta-percha and amalgam, and the animals were observed, together with controls, for from two to twenty-four months. Highly specific results were obtained in this series of experiments. Thus of 34 dogs in which the teeth were infected with streptococci from foci of infection and the urine of nine cases of nephrolithiasis, 26 dogs (75 per cent.) developed urinary calculi. Three (60 per cent.) out of 5 dogs inoculated in the teeth with streptococci from two cases of alkaline phosphatic cystitis developed similar calculi. Thirteen (65 per cent.) out of 20 dogs with teeth infected by streptococci from three cases of ulcer of the stomach developed ulcer of the stomach. Seven (47 per cent.) of 15 dogs whose teeth were infected with the diplostreptococcus from chronic ulcerative colitis developed ulcerative colitis. In no instance were lesions other than the specific ones observed in these experiments, but some strains had insufficient infecting power to produce the specific or other disease. Thus, out of 40 dogs whose teeth were inoculated with the streptococcus from sixteen cases of chronic arthritis, not one developed arthritis, nor did any of 38 dogs inoculated in the teeth with twenty-three strains of streptococci from one or more cases of cholecystitis, iritis, chronic encephalitis, spasmodic torticollis, chronic poliomyelitis, goitre, and abortion, develop specific lesions. Five (13 per cent.) showed small calculi in the kidney. Of 1,014 control dogs, the teeth of which were not inoculated, and which were kept and fed in the same way at the institute, 51 (5 per cent.) revealed small urinary calculi, and 6 (0.6 per cent.) ulcer of the stomach.

The relation of the respective streptococcus to the disease produced was substantiated by demonstrating its presence microscopically in the specific lesions and granulomas about the teeth, and by proving that the streptococci isolated from the focus at the apex of the tooth and systemic lesion had, at the end of the experiment, retained specific or elective infecting power. The teeth, rendered pulpless, remained firmly in the jaws; they apparently caused no pain, but became opaque and dark in colour. At the apices, areas of rarefaction were found filled with granulation tissue. The disease produced, especially in chronic ulcerative colitis, ran a typical clinical course, the experimental lesions being essentially like those that occur spontaneously in patients. Sections of the granulomas produced experimentally were often indistinguishable, both as regards the character of the cellular infiltration and the diplococci, from

those that develop so commonly about the apices of pulpless teeth in human patients. In the dogs that developed systemic disease, as in patients having chronic disease, the antibody content of the serum was low. The tooth from which the pulp was merely removed often became infected with the streptococcus inoculated into the other three teeth rendered pulpless. The foci produced experimentally with different streptococci, besides giving rise to the specific disease characteristic of the streptococcus inoculated, had other more general deleterious effects. The dogs lost weight and hair, and became highly susceptible to intercurrent infections. A dietary and other living conditions adequate to maintain health in normal control dogs was inadequate for the dogs in which chronic foci were produced experimentally.

In order to throw some light on the mechanism of elective localization, we have injected animals simultaneously with the living cultures, with the corresponding heat-killed bacteria (60° C. for thirty minutes) in larger amount, and with the filtrate of rapidly growing broth cultures. In this way we have found that streptococci having elective localizing power develop in their protoplasm, and set free in the broth, toxins or poisons which injure electively the very tissues in which the living streptococcus becomes localized and produces lesions. This has been shown especially in the case of streptococci from myocarditis, endocarditis, ulcer of the stomach, and epidemic hiccup. An interesting point emerged—namely, that after the living culture had lost the power to localize electively from artificial cultivation or successive animal passage, the dead bacteria and filtrates also no longer had specific effects.

On the basis of our clinical observations and experimental results, a focus of infection which for mechanical reasons cannot heal or drain should be regarded not only as a place affording favourable conditions for entrance into the blood, or lymph stream, of bacteria and their toxic products, but as affording also conditions (relative lack of oxygen, mixture of bacteria) favourable for the bacteria to acquire and maintain peculiar and relatively high infecting power. The focus makes for a forced relationship between living bacteria and the resisting mechanism of the host. Since the bacteria, usually streptococci isolated from foci, have been shown to possess elective localizing power, to contain and produce specific poisons and antigens, and the properties which may render the host and the tissues in which they localize hypersensitive or allergic, the importance of the focus cannot be ignored in any phase of a study of the etiology, pathology, immunology, and treatment of a large number of infective diseases. Since immunity to streptococcal infections is of short duration, the focus will need to be considered even after highly specific curative vaccines and serums are discovered and successfully applied. The importance of high resistance from proper living in the maintenance of continued health is taken for granted.

Devitalization of teeth and the filling of root canals, practised as a routine in the past, at any rate in America, should cease. It is to be hoped that efficient methods will be found that will not only sterilize pulpless teeth and periapical tissues that have become infected, but will also prevent subsequent infection, especially of the periapical tissues. The fulfilment of the latter requirement seems almost unattainable, and until this has been accomplished by the newer methods now being introduced, and which appear more promising, it would seem wiser to remove teeth that have become infected, or that require extirpation of the pulp, than to retain them at the risk of having them become the source of an insidious infection later. Normal vital teeth, free from pyorrhoea, pulp stones, and fillings, should never be extracted, except when necessary for restorative work, but the extraction of pulpless teeth seems to me to be indicated, regardless of the appearance of the x-ray photographs. It seems to me also that tonsils should be removed, regardless of whether they are large or small, or whether they are visibly infected or not, unless this is contraindicated for various reasons, in all patients who have serious systemic diseases presumed to be of focal origin, and provided that no other focus can be found. It must not be supposed, however, that other regions, not in any sense foci, may not also harbour the streptococcus with which the disease from which the patient is suffering may be reproduced. We have isolated streptococci in some instances, not only from foci, but also from the more normal mucous membranes of the upper part of the respiratory tract, and from the stools. This may explain why the condition of some patients does not improve following the removal of one focus or more.

It also goes to show that our conception of the principle embodied in focal infection must not be too mechanical. The bacteria that gain entrance through foci must overcome the same inherent resistance of the host as those that gain entrance elsewhere; the factors determining their localization are the same in both instances.

In the demonstrated fact of focal infection and elective localization there is nothing incompatible with the broadest possible concepts regarding the importance of other and more general factors at work in the causation of disease. It does not at all minimize the importance of peculiarities in the host, such as those due to inherited constitutional predispositions, to allergy, to undue fatigue and exposure, to alcoholism, and to intercurrent infections. Indeed, our newer work emphasizes the importance of these, and reveals more clearly how they are operative.

The streptococci isolated are believed to have etiological significance because they have been almost constantly demonstrated in foci and, when available, in the affected tissues. They possess on isolation elective localizing power and the characteristic cataphoretic potentials. The different diseases have been simulated by various methods of injection of freshly isolated strains, and some diseases have been accurately reproduced with the respective streptococci through chronic foci such as occur commonly in human subjects. Most of the strains from the different diseases studied are agglutinated specifically by the respective hyperimmune serums prepared in horses, and which possess curative properties in several of the diseases arising spontaneously in man, as in those experimentally induced in animals with the respective streptococcus.

E. C. ROSENOW.

## THE RESEARCH DEFENCE SOCIETY.

### ANNUAL MEETING.

LORD LAMINGTON presided at the annual meeting of the Research Defence Society on June 3rd, when the annual report of the committee was presented. The fourth Stephen Paget Memorial Lecture was delivered by Mrs. Mellanby, her subject being the value of animal experiments in determining the question of diet and dental disease.

The committee, whose report was presented by Lord KNUTSFORD, pointed out that the Home Secretary (who was himself on the list of vice-presidents of the British Union for the Abolition of Vivisection) had expressed the opinion that, in view of the thorough investigation by the Royal Commission, which reported in 1912, there was no call at present for further inquiry. This was precisely the attitude taken up by the Research Defence Society, and now that it came from a man who in private life was an antivivisectionist, but who by virtue of his office was in a position to inquire into the true facts, it deserved wide notice. The main trend of antivivisection endeavour during the year had been propaganda against the appeal of the Royal Veterinary College, and against the work of the Medical Research Council. With regard to the former, the society had exposed the absurd position whereby, on the one hand, antivivisectionist societies stood for the prevention and alleviation of animal suffering, while, on the other, they spent their funds on campaigns against the progress of veterinary medicine. As for the Medical Research Council, it was well to remember that, apart from the valuable researches conducted by that body, it had been responsible for some time past for the maintenance, and, in some cases, the development, of the national biological standards for certain drugs and preparations of the utmost value in everyday practice.

Sir LEONARD ROGERS, the honorary treasurer, had no very encouraging report to present. The society had been obliged to realize some of its invested capital in order to meet expenditure; an appeal was made for increased regular annual subscriptions.

### *Stephen Paget Lecture.*

Mrs. MELLANBY'S Stephen Paget Lecture, which was illustrated by lantern slides, recounted her well-known work on the study of the teeth. Mrs. Mellanby confessed that she had started as an antivivisectionist, but, like other antivivisectionists, she knew nothing about the matter

except the stories she had heard. At Cambridge, however, she found herself unable to continue her work without taking part in a vivisection experiment; she had since seen thousands of so-called vivisection experiments, and had come to realize what "a humane crowd of people" were those who were thus engaged. A very large proportion of the total experiments on animals were feeding experiments, though for these, as for others, it was necessary to have a licence, and an inspector was entitled to pay unannounced visits. The work she had to describe, from which results of advantage to children particularly had emerged, entailed the feeding of animals on experimental diets, with the object of ascertaining the effect of variations of feeding upon the structure and arrangement of teeth. She mentioned that the animals were kept in large cages, which were cleaned out every day, and had a bed lined with shavings. In attempting to find out the effect of any one set of conditions animals of the same litter were used, the diets were started at the same time, and the animals killed at the same time. The value of vitamin D in the calcification of teeth was illustrated by a photograph of the jaws of four puppies whose permanent teeth were just beginning to develop. The diet of all four consisted of lean meat, separated milk, white flour, a little orange juice, and a little yeast, the only difference being in the type of fat given. The fats were respectively salad oil, butter, egg yolk, and cod-liver oil. With the first of these food-stuffs the structure of the teeth was extremely bad, with the second and third it was good, and with the fourth it was best of all. Vitamin D was absent from salad or linseed oil, and present in abundance in cod-liver oil.

Turning to the structure of human teeth, the lecturer said that it was usually believed that the milk teeth of children were well calcified; but animal experiment had suggested that this could not be widely true, and the result of examining the teeth of a large number of children had convinced her that a very large proportion of children in this country suffered from defective calcification, especially of the milk teeth. In more than 600 cases she found only 1 per cent. in which the milk teeth were nearly perfect, and in 29 per cent. they were very defective. A question arose whether the beginning and spread of decay in human teeth could be influenced by diet after the teeth were fully formed. The experiments had shown that after the structure of teeth was established, diet could influence the spread of decay. The proper diet might not be able to arrest decay, though sometimes it did. Mrs. Mellanby also spoke on the presence of pyorrhoea in animals; dogs suffered greatly from this complaint, and the period of early development was of the greatest significance from the point of view of subsequent pyorrhoea. In conclusion, Mrs. Mellanby said that in the work she had described, experiments on animals had been the means of leading to a better understanding of the facts of human dentition. Experiments on animals and investigations on human beings had been intermingled in this research, but, of course, it had to be remembered that only beneficial influences could be tested on man. The worst errors in feeding, especially of children, were now known, and permanent improvement only became possible as a result of animal experiment, which could never have been undertaken if a small section of the community had had its way.

At the conclusion of the lecture a lady in the audience desired to put some questions to Mrs. Mellanby, but these were disallowed by the chairman as irrelevant. The proceedings closed with a vote of thanks to the lecturer, proposed by Lord KNUTSFORD, who commented upon her combination of expert knowledge and disarming modesty.

THE annual meeting of the American Medical Association will be held this year at Detroit from June 23rd to 27th, under the presidency of Dr. William Gerry Morgan of Washington. The scientific proceedings have been organized in fifteen sections. A special feature of this meeting will be the presentation of symbolic medals to ex-presidents of the Association. All the eighteen past-presidents now living, except Dr. W. W. Keen who is 95 years of age, will attend in person to receive the emblem. A portrait of each appears in the special Detroit number of the *Journal of the American Medical Association* dated May 24th.