Fig. 2. X-ray diagrams of (a) a normal site, (b) a fibrinoid site in a rheumatoid subcutaneous nodule

Fig. 3. Electron micrographs of (a) a normal site, (b) a fibrinoid site in a rheumatoid subcutaneous nodule. $\times 9,050$

exploration by X-rays: it had collodion windows, and it was graduated vertically and horizontally in millimetres, so that when fitted into slides on the spectrometer the co-ordinates of the X-ray beam with respect to the slice could be read off directly for every photograph taken.

For the purpose of relating the X-ray co-ordinates to the topography of the adjacent fore-and-aft histological sections, a negative photographic plate was made of the slice in its carrier (Fig. 1a), and this was projected on to enlarged prints of the photomicrographs of the sections. When the best superposition of the two images had been obtained, the co-ordinates inscribed on the carrier were marked also on the prints (Fig. 1b).

The slice was explored with an X-ray beam $\frac{1}{2}$ mm. in diameter, photographs being taken of up to as many as thirty different spots. After the X-ray study was complete, tiny fragments were dissected out from each of the same spots and examined in the electron microscope.

Results

Detailed findings will be published at a more advanced stage of the investigation, which is being planned to include an inquiry into whether there is any detectable change in the pathological collagenous tissues corresponding to the dramatic alleviation of symptoms brought about by treatments with adrenocorticotrophic hormone (ACTH) and cortisone. It will suffice here to state that the sampling technique just described has proved very satisfactory indeed, and that we have found excellent correlation between the indications of histology, X-ray diffraction and electron microscopy. We have obtained two limiting X-ray

diagrams: one (Fig. 2a) of normal collagen (often oriented and with, of course, the liquid halo in addition), corresponding to regions which histology also would specify as normal; and the other (Fig. 2b) consisting of little more than a diffuse ring of spacing about 4.8 Å. This latter diagram we definitely associate with the histological fibrinoid regions—a poor name, by the way, since there is no recognizable X-ray evidence so far of the presence of true fibrin, for which we should expect either an α - or a β -diagram. For many of the spots examined the X-ray photographs showed both diagrams present at the same time, in general one or the other predominating in correspondence with the histological indications. In one region of a slice we found that it sufficed for the X-ray beam to be moved through only $\frac{1}{2}$ mm. for the normal collagen diagram to disappear entirely and be replaced by the pure fibrinoid diagram.

The electron micrographs also revealed two limiting conditions: one of apparently normal collagen fibrils (Fig. 3a), and the other of amorphous material. Mostly, however, there was seen a mixture of the two, though again, in general, one or the other predominated in correspondence with the histological and X-ray indications. Fig. 3b is a typical picture of an intermediate state.

Concurrently with this special investigation on rheumatoid arthritis, we at Leeds have been collaborating with Prof. R. E. Tunbridge and other colleagues at the Medical School in a wider survey of pathological collagenous and related tissues. From this work it is clear that the real problem in the end is to characterize the degenerate fibrils and amorphous materials that are found so frequently in all sorts of clinically different conditions. Though they look so alike in the electron microscope, they can scarcely be the same every time, and the next step must obviously include comparative chemical analyses. We have already made a beginning along such lines in the rheumatoid arthritis problem, and we hope soon to be able to supplement our correlated histological, X-ray and electron microscope findings on slices of subcutaneous nodules with a corresponding set of micro-biochemical results.

We should like to thank Mr. G. Eaves for assistance in the electron microscopy and Mr. A. Millard for the photographic reproductions.

OBITUARIES

Prof. W. E. Agar, C.B.E., F.R.S.

WILFRED EADE AGAR, emeritus professor of zoology in the University of Melbourne, died on August 14, aged sixty-nine. His health had been precarious through cardiac trouble since 1943, and he had to lead a more and more sedentary life; but he continued to work quietly in his little home laboratory up to the day before he died.

Born on April 27, 1882, at Wimbledon, Agar passed from his preparatory school to Sedbergh and then to King's College, Cambridge, where his tutor was S. F. Harmer. He went through the regular courses of instruction for the Natural Sciences Tripos, Parts I and II, in both of which he obtained a first class. Of all his teachers he looked back with special gratitude to Harmer, for his inculcation of precise and orderly method, and to Bateson, then in the flood tide of Mendelism, for turning his mind in the direction of his future research in genetics.

I had been impressed by Agar as the most outstanding member of the Tripos class in zoology during my last year as demonstrator; so when he had completed his Tripos, I invited him to join the staff of the Zoology Department in the University of Glasgow, on which he remained until 1920, holding latterly the position of senior lecturer.

During his Glasgow years, Agar showed himself to be an admirable teacher, and he also achieved a large proportion of his most valuable research work. During his first two years this was devoted to vertebrate morphology, and he produced valuable papers upon the skull and visceral arches, and upon the anterior mesoderm, of *Lepidosiren* and *Protopterus*. In 1907 he made an expedition to the Gran Chaco to supplement my work on *Lepidosiren*; but above all to obtain full material for investigating the gametogenesis of that fish—outstandingly suitable for such a research on account of the relatively enormous size of the chromosomes and their strongly marked individuality. Agar made a splendid success of his expedition and brought back a large amount of perfectly preserved material which he proceeded to investigate in detail. His skill and accuracy as an observer, in conjunction with his admirable technique, enabled him to achieve what is still probably the most reliable account of the gametogenesis of a male vertebrate. In his work he made full use of the Glasgow technique, which enjoined that all microscopic work under high-power oil-immersion objectives be done with stereoscopic eyepieces—the technique which enabled Ballantyne in 1925 to establish with certainty the passage of neurofibrils across the generally accepted discontinuity between the neurones of the vertebrate nervous system. Agar's Chaco expedition achieved other results than those of his main quest, the most important being the discovery of the 'neonychium'—the cushion-like structure which in the embryo of the Amniota fills up the concavity of the claw and safeguards the amniotic membranes against injury.

Agar's work on the chromosomes of *Lepidosiren* may be said to inaugurate the second phase of his research career, devoted to genetics. Next after it came the breeding through long series of generations of Daphnid crustaceans and having as their main object the testing of Lamarckian inheritance of environmental or 'acquired' characters. The Daphnids in question were chosen as specially advantageous for such investigations in view of their parthenogenetic reproduction, their short life-cycle, and the fact that all members of a clone are genetically identical so as to exclude the disturbing effects of Mendelian segregation. The results of Agar's work on the whole, including one particularly precise set of experiments extending over a hundred generations, was to show the complete absence of any evidence of such inheritance.

Both by his own original work and by his critical examination, and in some cases repetition, of the

work of others, Agar played an important part in substantiating the view that environmental or 'acquired' characters are not inherited and are therefore not available for the process of racial evolution.

In its third phase, Agar's work diverged from the realm of pure science, in which things are observed, accurately recorded and when possible seriated into a general expression, into the realm of 'philosophy', which deals rather with ideas or opinions, and is free from the constraints to which purely scientific research is subject. In this phase Agar was, above all, influenced by the philosophy of A. N. Whitehead—primarily a mathematician, not a biologist—as expounded in his "Process and Reality". According to this philosophy, reality consists not in substance but in process, and the difference between living and non-living 'organisms' is merely one of degree—"Biology is the study of the larger organisms; whereas physics is the study of the smaller organisms." Whether or not Whitehead's philosophy is destined to have any influence upon the advancement of biological science, it is clearly of advantage to have an account of it and its implications from the pen of one who not only accepts the general principles of that philosophy but also holds a distinguished position in the realm of biological science. Such an account with further developments in detail is provided by Agar in his last book, "A Contribution to the Theory of the Living Organism" (Melbourne University Press, 1943), a revised edition of which he had just completed at the time of his death.

It would be wrong to conclude this notice without mention of Agar's activities outside laboratory and lecture-room. At Glasgow he held a commission in the Officers' Training Corps, and during the First World War he was captain in the 5th Highland Light Infantry, until invalided home from Gallipoli. Later he acted as adjutant to the 1st Volunteer Battalion of the same regiment. Then in 1920 came his appointment to the professorship of zoology at Melbourne. There he served as dean of the Faculty of Science (twice), president of the Professorial Board, in which he played an important part in the deliberations preceding the appointment of a full-time vice-chancellor, and as member of the University Council (twice).

As a Melbourne colleague writes, "Wilfred Eade Agar will be remembered by all as a thoughtful and kindly man, reserved, yet with a delightful sense of humour, slow to assert himself, yet vehement when the need arose. With his death the University of Melbourne has lost one of its great men."

JOHN GRAHAM KERR

Brigadier E. M. Jack, C.B., C.M.G.

BRIGADIER EVAN MACLEAN JACK, who died on August 10, was born in Edinburgh in 1873. Commissioned in the Royal Engineers in 1893, he served first at Gibraltar and St. Helena; and in 1903 joined the Ordnance Survey, on the staff of which he served for four years.

In 1907 he was selected for duty with the Uganda-Congo Boundary Commission under Major Bright and four years later became chief commissioner of another Central African Boundary Commission, which, in the course of its work, measured a section of the arc of the 30th meridian. In 1913, Jack, now promoted major, was posted to the Geographical Section of the General Staff at the War Office; and on the