to the nineteenth century, as well as the names of the staff and students and their activities during the years of the School's existence from 1941 to 1949.

The first part, which includes an account of the careers of two learned Scotsmen in Poland, Drs. John Johnston (1603–1675) and William Davi(d)son (1593–?1669) and a valuable English and Polish bibliography drawn from little-known sources, will be of some interest to medical historians. The details of the School's eight years at Edinburgh may be of use to historians in the future.

The whole forms a worthy memorial to an unusually imaginative act of co-operation, and is admirably edited, printed, and illustrated.

ROBIN PRICE

Lectures on the Comparative Pathology of Inflammation, by ELIE METCHNIKOFF, translated from the French by F. A. Starling and E. H. Starling, with a new introduction by Arthur M. Silverstein, New York, Dover Publications, 1968.

Immunity in Infectious Diseases, by ELIE METCHNIKOFF, translated by F. G. Binnie, reprinted with a new introduction by Gert H. Brieger, New York and London, Johnson Reprint Corporation, 1968, pp. xxxi, xvi, 591, illus., $25.00.

The Dover reprint of Metchnikoff's *Lectures on the Comparative Pathology of Inflammation* is nicely supplemented by the Johnson reprint of his *Immunity in Infectious Diseases*. The *Lectures* first appeared in French in 1892, and *Immunity* appeared nine years later. In the period between Metchnikoff had been engaged in extending the territory claimed by his theory of phagocytosis and defending its already threatened borders. Although Metchnikoff's ideas had been frequently enough attacked in the 1880s the *Lectures* are unmarred thereby, and in reading them we share something of his original enthusiasm for his new insight into the mechanisms of the protective response up and down the scale of animal life. In contrast the *Immunity* reads somewhat like a legal document. It is crammed with claims, refutations and counterclaims: the reader breathes in an atmosphere that after a while becomes a bit stifling. Metchnikoff's tone toward his adversaries is usually mild, although the intensity with which he experienced their attacks may be measured by his later comment that the 'polémique à propos de la phagocytose aurait pu me tuer ou m'affaiblir définitivement bien plus tôt. Par moments . . . j'étais prêt à me débarrasser de la vie' (Elie Metchnikov, *Souvenirs,* Moscow, 1959).

The reader of *Immunity in Infectious Diseases* will find in it no brilliant new insight of the kind that illuminates the *Lectures*. For Metchnikoff's theory of immunity is co-extensive with his theory of inflammation. Both are aspects of his theory of phagocytosis, a theory comprehensive enough to embrace in addition the metamorphosis, healing, atrophy and ageing of tissues, the greying of hair, even macrobiosis and preventive geriatrics. It was his co-worker Alexandre Besredka who first pointed out in detail that the varied aspects of Metchnikoff's work in biology and medicine—even including his ideas on the effects of intestinal intoxication and his 'optimistic philosophy of life'—were unified by his conception of phagocytic digestive activity (*Histoire d'une Idée, L'Oeuvre de E. Metchnikoff,* Paris, 1921). In the *Lectures* Metchnikoff had defined inflammation as a protective process mediated by phagocytes, cells that engulfed, digested and disposed of animate or inanimate irritants entering the body other than as food materials. The task in the simpler

forms of life was accomplished by cells wandering freely through the tissues. Moving lower and lower down the scale of life the distinction between inflammation and digestion became increasingly blurred. In one-celled organisms it could hardly be made; the amoeba ingesting its food and consuming a foe were engaged in one and the same activity. Because of its survival value the inflammatory process had been retained and further developed, so that in the course of time a complicated interplay of the nervous and vascular systems in man and the higher animals brought cells specialized in the uptake and digestion of foreign matter to points of attack or injury. These cells Metchnikoff christened 'phagocytes': the 'microphages' and 'macrophages' of the blood and tissues. In *Immunity in Infectious Diseases* he defined immunity as follows: 'When an animal remains unharmed in spite of the penetration of infective agents it is said to be immune'. Not too surprisingly he found the weight of evidence, assembled by himself and others, to indicate that 'phagocytosis . . . is sufficient to ensure natural immunity. The bactericidal power of the serum, which for a long time served as the basis for a humoral theory of immunity, represents merely an artificial property, developed in consequence of the setting free of the microcytase of the leucocytes that have become disintegrated after the blood has been drawn. The agglutinative power of the normal fluids of the body plays no important part in natural immunity' (p. 206). In acquired immunity, on the other hand, the presence and importance of bactericidal and agglutinative substances in the blood could not be overlooked. But here, too, we are dealing, said Metchnikoff, with 'special phases of intracellular digestion' (p. 299), for ' . . . in acquired immunity . . . also we have intracellular digestion with over-production of specific fixatives, part of which are excreted and pass over into the plasmas' (p. 296). Protective sera, according to Metchnikoff, act by virtue of microbicidal, agglutinative and fixative substances present in the body fluids or by stimulating phagocytic defence mechanisms and the latter is more important.

In his informative introduction to the Johnson reprint, Gert Brieger devotes several paragraphs to the claim of the American bacteriologist George Sternberg that in 1881 he anticipated Metchnikoff in stating the phagocytic theory of inflammation and immunity. Brieger notes that several other workers at about this time or shortly before had suggested that the white blood cells might act in defence of the body against invading agents of disease. He points out that Metchnikoff went out of his way to give due credit to these men in *Immunity in Infectious Diseases*. The earliest suggestion bearing on the protective activity of the white blood cells cited by Metchnikoff is that of Panum, whose only printed comments on the subject are buried in a footnote to a paper published in *Virchow's Archiv* in 1874. Metchnikoff did not mention the work of Sternberg or the still earlier dissertation of Muellendorf (1879), the latter apparently having been first brought to light by Robert Herrlinger 'Die historische Entwicklung des Begriffes Phagocytose', *Ergebn. Anat. Entwicklungsgesch.*, 1956, **35**, 334–57. If we agree to play the sometimes misleading game of 'precursor', it is possible to move back still further into the past. Observations on the uptake of particulate matter by cells can be traced back to the beginning of the nineteenth century, if not before, and the suggestion that white blood cells act somehow in a protective capacity is almost as old. To my knowledge no one has mentioned the Philadelphia pathologist Joseph Richardson in this context. In 1869, only two years

after the appearance of Cohnheim's essay *Ueber Entzuendung und Eiterung*, he confirmed the identification of white blood cells and pus corpuscles by the latter, equated both with mucus and salivary 'corpuscles' and, after identifying certain minute bodies in salivary corpuscles with Lionel Beale's 'germs of bacteria', argued that the white cells might have the role, by virtue of their amoeboid activity, of gathering up bacteria and conducting them beyond the confines of the body (*Penn. Hosp. Rep.*, Vol. II). But a protective, policing role had been attributed to cells even before the rise of the germ theory of disease in its modern form. The belief that pus contained a 'concocted' *materia peccans*, i.e. digested and rendered ready for discharge from the body, rests on a Hippocratic basis. With the discovery that pus contained 'corpuscles' together with the partial identification of free cells in multicellular organisms and free-living unicellular organisms it might easily have occurred to someone that the pus corpuscles themselves were engaged in the disposal of the *materia peccans*. And in fact we find Virchow in 1847 rejecting as anachronistic precisely this view. 'We no longer', he wrote, 'regard the pus corpuscles as gendarmes ordered by the police-state to escort over the border some foreigner or other who is not provided with a passport'. One wonders whether Virchow, as he encouraged Metchnikoff to continue with his studies on phagocytosis during their encounter at Messina, thought of his own earlier statement. Or did he perhaps only later, when he read these lines by Metchnikoff?—'Nature rids the mucous membranes of the skin of a large number of micro-organisms, eliminating them by epithelial desquamation, and expelling them along with fluid secretions and excretions . . . She is constantly sending to the mucous membranes and the skin an army of mobile phagocytes which explore the ground and rid it of micro-organisms' (*Immunity in Infectious Diseases*, p. 432). But while it is easy to point to intimations of Metchnikoff's *idée directrice* (as Besredka called it) before his time, it is almost as erroneous to measure these intimations against the richly thematized and developed corpus of his life work as it would be to suppose that the occasional use here and there of a fourth paeonic foot entitled the user to claim a share in the composition of Beethoven's fifth symphony.

The question of the polemic that accompanied Metchnikoff's presentation of his views is worth additional comment. Part of the antagonism that he stirred up in medical circles was indeed a consequence of his lack of acquaintance with 'intimations' of the kind mentioned above, together with his oversimplification of complex issues. As a biologist he was at first both relatively uninstructed in what had already been done along the lines of his own approach and ignorant of medical and pathological theory. As late as 1902, in the long and otherwise excellent historical essay that forms the penultimate chapter of *Immunity in Infectious Diseases*, he was capable of writing that pathologists in 1882 'regarded inflammation as the consequence, if not always, at least in the majority of cases, of the penetration of micro-organisms.' In fact, that hypothesis was only beginning to obtain credence, especially among bacteriologists. Elsewhere it played a subordinate role. Metchnikoff was unaware, when composing the *Lectures*, that inflammation had often been interpreted by successive generations of pathologists and medical men as a protective process. Most recently, this had been done in the 1870s to Naegeli and Buchner, who attempted to show that inflammation was a manifestation of local tissue resistance against

invading organisms (Naegeli and Buchner are however cited in *Immunity in Infectious Diseases*). Even the phrase 'salutary reaction' (*Immunity*, p. 513) can be traced back via John Hunter to its first appearance in the writings of Georg Stahl's pupil Michael Alberti, where it appears as *actus salutarius;* the idea itself is of course much older. As for the oversimplification inherent in Metchnikoff's generalization, it could not escape the comment even of those who were favourably disposed toward his work. But a part of the antagonism must be attributed to the covert and sometimes open scientific chauvinism displayed by German and French scientists after 1870, as Metchnikoff himself knew (cf. *Immunity,* p. 536). How long its effects persisted can be seen from a perusal of French and German textbooks of pathology from 1890 down to the present. Some German pathologists even went so far as to attribute the idea that inflammation involved a digestive act to Roessle, rather than to Metchnikoff, although Roessle's work came a generation or more later and he himself called attention to the neglect of Metchnikoff's ideas in German circles. The balance, incidentally, was somewhat redressed by Herrlinger in the article referred to, where seven out of the total of sixty bibliographical references are to the work of Metchnikoff.

In spite of the limitations that have had to be placed on Metchnikoff's view of inflammation and immunity, the *Lectures,* at least, constitute one of the great medical and biological classics of modern times. And this is not because, as is sometimes said, Metchnikoff introduced the comparative biological method into medicine. Anyone familiar with the nineteenth century medical literature, with the work of Johannes Mueller and Koelliker in Germany, for example, or of Carpenter and Gulliver in England can hardly accept that claim without qualification. What Metchnikoff did do was to apply the comparative method, in the light of evolution and natural selection, to the study of a particular set of pathophysiological events traditionally grouped under the heading of inflammation and by this means define the essence of the process. No one before him had so thoroughly shown the connection between extracellular and intracellular digestion and the relation between digestive, protective and immune processes. One final remark: in view of current work indicating that in certain immune inflammatory processes the neutrophile leucocytes, after having been attracted by the presence of antibody-antigen-complement complexes, may be acting to produce rather than prevent tissue damage—where, to revert to Virchow's metaphor, the police are rioting rather than protecting the peace—it is worth noting that phagocytosis was, for Metchnikoff, not a protective process in all of its aspects. While he regarded the phagocytosis occurring in inflammatory and immune processes as protective, in the later development of his ideas he reached the conclusion that phagocytosis was also the mechanism involved in the pathological ageing of tissues (cf. *The Nature of Man, Studies in Optimistic Philosophy*, London 1903). When the balance between the aggressive phagocytic cells of the body and the more highly developed parenchymal and nerve cells was upset by the effect on the latter of 'intoxicant' substances (derived, according to Metchnikoff, from the bacteria of the large intestine) a kind of internecine warfare took place in which the phagocyte was the victor and the battlefield transformed into fibrous tissue. So even here we can, if we wish, see a bridge of sorts between the old and the new.

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