EDITORIAL

On pages 29-37 we have abstracted as fully as space permits a book called *Experimental Tuberculosis, Bacillus and Host, with an Addendum on Leprosy*. It includes 25 papers (along with discussions) which were read at a symposium called by the Ciba Foundation in October, 1954. The papers may be roughly divided according as they deal with the tubercle and leprosy bacillus, or with the monocyte or phagocytic cell which seeks to destroy the bacillus. For, though other factors come into the picture, the real issue is the struggle between the bacillus and the cell which engulfs it. This cell, depending on its condition at the time, either grants the bacillus sanctuary and facilities for multiplication, or else destroys it. This dual bacillus-cell relationship, common to both diseases, is described by Lowe(2)* as " a curious dichotomy," and by Lurie(1) as symbiotic and nodular phases.

Taking the bacillus first, as being the aggressor, its composition is studied under proteins (5), lipids (8, 15), and polysaccharides(7, 8). While proteins are used in *testing* sensitivity to the tubercle bacillus, polysaccharides associated with lipids are becoming increasingly regarded as responsible for *causing* skin and cellular reactions and immunity generally(8, 15). Mycolic acids(6) (lipopolysaccharides) have been found to vary in their composition according to the virulence of tubercle bacilli. Mycolic acids are also supposed to be indirectly responsible for the acid-fastness of mycobacteria by participating in the formation of an impermeable surrounding film; and thus virulent mycobacteria are stained red with neutral red and avirulent stains yellow.

Virulence is also discussed in connection with the cord factor(12), which is partly responsible for virulence, and when injected in infected mice can cause a flare up and rapidly progressive disease.

Several papers deal with the important period when infection first takes place. When many bacilli are inoculated into an animal there is a discrepancy between the wide-spread lesions and the few acid-fast bacilli that can be detected. Is it possible that there is a granular or nonacid-fast cycle in the life of mycobacteria?(19). This is an important question which has often been raised in connection with *Myco. leprae*. The role of early tissue reactions in determining whether the host or the bacillus will win

* The numbers in the text correspond with the numbers of the abstracts on pages 29-37.

is shown by the use of adrenalin or "Liquoid"[10], which act as temporary inhibitors of defence reactions. The importance not only of response to infection but of sufficiently rapid and early response is shown in Hanks' paper[4]. It may be that B.C.G.[20] furnishes just this little extra resistance to turn the tables between progressive and arrested infection. Hanks'[4] suggestion of mixing dead lepra bacilli with the living B.C.G. vaccine for increasing the possible protective power of the latter is worth following up.

It is questioned[13] whether the serological differences between the different antigenic constituents of culture filtrates of the tubercle bacillus are of any specific significance in relation to tuberculous disease. It is suggested[14] that the haemagglutination test indicates only an enhancement of a non-specfic reaction. In leprosy, in the lepromatous type with abundant bacilli, there are plenty of circulating antibodies but, as is shown by the lepromin test, there is no sensitization and no resistance to infection; while in the tuberculoid case, where these signs of resistance are found, antibodies in the blood are difficult to find[2].

If we pass from the bacillus to the phagocytic cell (monocyte or macrophage), what are the factors which determine resistance, or the symbiotic versus the nodular phase? Suter[17] shows by *in vitro* study that in tuberculosis after vaccination the growth-inhibitory power of monocytes is independent of hypersensitivity, although both of these appear at about the same time. He shows that hypersensitivity along with large numbers of bacilli in the cells seems to favour multiplication of bacilli; whereas if the bacilli are few, hypersensitivity allows full inhibitory power to the cells. Does this correspond to the well-known phenomenon in leprosy, where the acute exacerbation (lepra reaction) in the lepromatous type (where there are many bacilli) is followed by the disease getting worse, whereas in the acutely reacting tuberculoid (where there are few bacilli) the result is not infrequently a spontaneous clearing up of the lesions?

Various substances, such as fatty acids, have the power to produce the "nodular phase" with its follicular formation, epithelioid and giant cells, and caseation [9]. But comparatively large quantities are necessary as compared with the follicle-producing power of a single bacillus, be it that of tuberculosis or leprosy.

The effects of cortisone on the monocyte are instructive[21] in its power to inhibit multiplication of bacilli, though not to inhibit phagocytic power. To what extent is the type of leprosy influenced by the endocrine system?

The effect of INH[23] in producing metaplasia, destruction of bacilli, and epithelioid and giant cell formation, may be contrasted with the results of sulphone treatment in lepromatous leprosy. Does something of this nature occur when the border-line type heals up promptly under treatment?

The effect of surface-wetting agents[24] in experimental tuberculosis opens up new possibilities. Leprosy workers in search of more effective forms of treatment will watch with interest for further results.

* * * *

In the *British Medical Journal* (Nov. 5, 1955, p. 1106) certain substitutes for B.C.G. are mentioned. Among these is Salvioli's "V.D.S." diffusing vaccine which consists of a mixture of heat-killed human and bovine tubercle bacilli with hyaluronidase added to it. This has been used extensively in Italy where it is found that the hyaluronidase produces in the dead bacilli a migratory property characteristic of living organisms, and indeed produces lesions in the regional lymph nodes that are not seen when dead bacilli are used alone. It may be worth while testing this vaccine as to its power to turn a negative into a positive lepromin reaction. If it has this effect to the same degree as B.C.G., further tests would be called for to determine its possible use in the prophylaxis of leprosy. There would appear to be less risk with a dead than a living vaccine. Also there would be additional advantage in primitive field conditions, far from adequate laboratory facilities, where it is difficult to maintain living cultures.