never attempted to carry, are now available for distribution.

CONSTRUCTION has been started for the new chemical research laboratory at Brown University, which has been made possible through a gift of $500,000 from Jesse H. Metcalf, formerly United States senator from Rhode Island, a member of the Board of Trustees. The laboratory will provide facilities for research in photochemistry and electrochemistry. Architecturally, it will harmonize with the early Georgian design of other buildings on the west campus. The outside will be brick with white stone and wood trim, 130 feet long, 48 feet wide and 54 feet high. It will adjoin the Jesse Metcalf Memorial Chemical Laboratory, named for the father of Mr. Metcalf. There will be sixty-one rooms for research, conferences, offices and for special technical purposes, accommodating between 30 and 40 graduate research workers. Facilities at the university for advanced chemistry will be doubled when the building is finished. There will be a new divisional library of 60,000 volumes capacity on chemistry, physics and mathematics. Some of the laboratories will be air-conditioned. The largest laboratory will be used for undergraduate instruction in physical chemistry.

DISCUSSION

TUBERCULOSIS, LEPROSY AND OTHER DISEASES CAUSED BY ACID-FAST BACTERIA[1]

THE purpose in preparing this symposium and in publishing in monograph form the papers composing it is to bring into prominence a disease process caused by a group of micro-organisms which, while closely grouped as a family, are yet separated by cultural, chemical, morphological and biological attributes. This family is called the *Acid-Fast Family* for simplicity's sake because all its members, those that cause sickness and those that cause no sickness, have the attribute of retaining dye when attempt is made to bleach this out with an acid or other decolorizing solution. They are called in scientific literature *Mycobacterium,* a genus of the *Mycobacteriaceae* family.

The members of this acid-fast family which are great producers of disease in man are the various strains of *Mycobacterium tuberculosis,* which cause tuberculosis, and of *Mycobacterium leprae,* which cause leprosy. In the animal kingdom various strains of the tubercle bacillus attack our food supply by producing tuberculosis in cattle, fowl, swine and other species. There are also strains of the tubercle bacillus which cause disease only in cold-blooded animals and live only at lower temperatures than are found in the bodies of warm-blooded animals. The Johne's bacillus, another member of this family, also takes heavy toll among cattle and allied species. Bacteria apparently allied to the leprosy bacillus cause a leprosy-like disease in rats and other rodents.

In addition to these disease-producing strains there are numerous strains of the acid-fast family which do not produce disease, for example, the timothy grass bacillus, which lives in the soil or on grasses, or the smegma bacillus, which dwells about the genitals of humans and some animals. Hagan, Rhines and others have succeeded in cultivating many strains of acid-fast bacteria from the soil.

The most striking common feature of the disease process caused by all those strains of the acid-fast family which cause sickness is that, regardless of whether the disease is fatal or not, the germ for part of its life history thrives inside of one cell of the body, known as the monocyte. This monocyte wanders about the body by its own motive power or is transported by blood and lymph stream. It may even carry the germ into the body from the outside, for example from the air passage. Later, rendered sluggish by the germs multiplying within it, the monocyte may stop in any part of the body, and where it stops disease may arise.

There are localities, different in different animals, where apparently the monocyte has special functions to perform. Such places are the lungs, the lymph glands, the gut, the spleen and the liver. As an illustration of this (and this is only one factor in the whole story) various strains of the human tubercle bacillus cause tuberculosis in man most frequently in the lungs, where monocytes are very abundant. This means that the monocytes found in the lungs perform some special function there, which probably means that they have likewise some very delicate or special internal chemistry. It does not require a great stretch of the imagination to conclude that in the early life history of this symbiosis between bacillus and monocyte there is some chemical factor that is common to both through which they contend for the same food supply. The same conclusion is logical about the monocytes of the lungs of cattle and strains of the bovine tubercle bacillus, the monocytes of the large gut of cattle and the Johne's bacillus, the monocytes

[1] Statement introducing the monograph of the American Association for the Advancement of Science, containing the papers presented in the Denver symposium, now in press for publication by The Science Press.

of the skin and nerve sheaths and the lepra bacillus in human leprosy, and so on, through other examples in different species of animals and different strains of acid-fast bacilli.

What the chemical factor is, has, up to now, eluded the investigator, possibly because of the difficulties surrounding the study of the internal chemistry of the monocyte, which does not thrive away from its natural environment in association with the other cells of the body.

Much progress, however, has been made in the study of the chemical processes involved in the life history of the various strains of acid-fast bacilli. The study of the chemical composition of the different strains of bacilli has yielded substances common to the whole family in the three gross divisions of their living tissues, that is, the proteins, the carbohydrates and the fats. This progress has been facilitated by our ability to grow many of the strains of acid-fast bacilli on a simple inorganic food stuff out of which each strain can make, by virtue of its own peculiar living characteristics, its own peculiar tissues. This study of the chemical processes has served to prove that the family is bound together by other bonds than acid-fastness and monocyte-bacterial relationship. And it has also served to isolate some of the distinctive qualities that make the strains what they are, *viz.*, human, bovine, or avian tubercle bacilli, timothy grass bacilli, Johne's bacilli, or leprosy bacilli.

From the same study have been found fractions responsible for the changes the bacilli themselves produce in disease, for instance, the fever, the skin reaction, the stimulation to multiplication and change in the character of the monocyte. The same studies have developed further knowledge on the difficult problem of virulence or the quality that certain strains of bacteria have for certain species of animals to produce severe or not very severe disease. It has been found, for example, that a single strain can be made more virulent at will by modifying the medium on which it grows, a phenomenon probably best exhibited with some of the avian tubercle bacillus strains, which can be made more or less fatal for the rabbit.

It is, however, in the later phases of the various diseases caused by these acid-fast bacteria that the contrasts between them become most marked in spite of their common early picture. The massive skin and nerve deformities of leprosy, the destructive cavity formations of tuberculosis, the stripped gut mucous membrane of Johne's disease, are as widely different pictures as possible, and yet with the microscope one finds the constant association of the acid-fast bacteria and the monocyte cell in all the diseases, even in these later phases.

In the blood serum of bodies infected by the different strains there is found also in immunological studies cross precipitation which binds the group together, but exhibits differences showing specificity as well. In the same way the skin reactions resulting from introducing proteins from the different strains into animals infected with one strain are similar and different mainly in the severity of reactions they cause.

This is of necessity but a short introduction to the substance of the papers which follow in this symposium. With the many similarities that have been pointed out, thought has been given to some word which will attempt to comprehend the diseases here described under a single term. Because the bacteria in the group are in scientific literature called *Mycobacteria,* Dr. Esmond R. Long has suggested the term "Mycobacteriosis," which serves the purpose admirably.

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METHEMOGLOBIN REDUCTION BY GLUTATHIONE OR CYSTEINE

GLUTATHIONE or cysteine is efficient, within the physiological pH range, in reducing methemoglobin to hemoglobin, which is able to combine reversibly with oxygen and carbon monoxide. The reduction has been accomplished *in vacuo,* in air, in hydrogen and in carbon monoxide. For example, in the presence of carbon monoxide and using cysteine as the reductant 1.0 millimole of added cysteine had effected the reduction of 0.6 millimole of methemoglobin (on a heme basis) in 24 hours at room temperature. The initial concentrations in this example were 0.14 millimole of methemoglobin and 0.16 millimole of cysteine per liter. Under identical conditions except for the reductant used, 1.0 millimole of added glutathione effects the reduction of 0.7 millimole of methemoglobin. When considerably larger relative concentrations of cysteine or glutathione are used reduction is complete and almost instantaneous whether in the presence of carbon monoxide, hydrogen or *in vacuo.* In air, reduction is not as complete, presumably because of partial oxidation of the reductant by the atmospheric oxygen.

The glutathione content of the human red cell is relatively high (about 40 mg per 100 cc. of whole blood) and is present almost entirely in the reduced form.[1] The ratio of oxidation-reduction equivalents of glutathione to total pigment in the normal red cell is therefore 1 to 5. It is also well known that when hemoglobin is liberated from the cell it is transformed

[1] S. R. Benedict and G. Gottschall, *Jour. Biol. Chem.,* 99: 729, 1933.