was about 1.5 gr. per 100 gr. of crude material when 2 extractions with pyridine were made.

From the pyridineinsoluble material a water soluble fraction similar to "A" was prepared, giving strong orcinol copper reaction and only weak complement fixation with heterogenetic antiserum. Substances of similar chemical properties as "A" could be obtained from beef kidney and beef brain.

This is a preliminary report.

[1] PROC. SOC. EXP. BIOL. AND MED., 1926, xxiii, 343-344; *J. Immunol.*, 1925, x, 731-733.

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Mononuclear Cells of Blood in Relation to Clinical Findings in Human Tuberculosis.*

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In 1925 a new hypothesis in regard to the propagation and resistance of tuberculosis was presented by Cunningham, Sabin, Sugiyama and Kindwall.[1] The data for their conclusions were obtained from a study of rabbits injected with viable bovine tubercle bacilli; differential blood studies were made throughout the course of the infection by the supra-vital technique of Sabin, and freshly autopsied material was examined by the same technique. They found that, during the course of a tubercular infection, the so-called "reticular cells" are stimulated to an increased production of monocytes and these in turn are transformed into typical epitheloid and giant cells. From a study of the appearance and number of the bacilli, which were found in the monocytes and in the epitheloid cells, they concluded that these cells phagocytize organisms but are unable to destroy them, and hence act virtually as culture tubes. The concept was thus advanced that the monocytes are stimulated, in tubercular infections in rabbits, to such an increase in number and in phagocytic capacity, that, inasmuch as they seem unable to destroy the bacilli, they aid in increasing and disseminating the infection. Furthermore, the authors showed that these changes became more

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marked as the disease progressed, and receded with improvement; and that, coincident with the numerical changes in the monocytes, the lymphocytes were effected in inverse ratio.

The same technique is now being employed in similar studies upon clinical cases of human tuberculosis. All of the cases so far studied have been patients in the Vanderbilt University Hospital, selected for study, irrespective of the site or grade of infection or age of the patient. Where cases are in the hospital sufficiently long, or where marked clinical changes occur, the progress is followed by repeated examinations; and whenever tubercular fluids are obtained for clinical reasons they are subjected to study by the supra-vital technique, as are also tissues secured by autopsy or biopsy. Furthermore, we are extending our study to such other types of disease entities as show any indications of changes in the monocytes or lymphocytes. And finally, intracutaneous tuberculin tests are made in conjunction with these studies.

The blood and tuberculin findings thus obtained are being analyzed against the various clinical factors such as history, duration, physical examination, progress, X-ray plates, laboratory findings, biopsy and autopsy reports and the result of animal inoculation.

We have studied about 50 cases up to the present time in which tuberculosis has been positively diagnosed or strongly suspected. From the analyses of these 50 human cases it has been found that cytological changes, similar to those reported in the rabbit with experimental bovine tuberculosis, occur in about 85 per cent of them. Those cases showing numerical and qualitative changes in monocytes and lymphocytes, comparable to the changes described in the rabbit, are usually those with pulmonary or disseminated tuberculosis; while only a smaller percentage of the more localized types of tuberculosis present characteristic blood changes. Moreover, the same variations, as those occurring in the rabbit during the course of experimental tuberculosis, have been found in the human cases in which the disease progress has been followed; *i. e.,* the numbers of monocytes rise and of lymphocytes fall as the disease progresses and the opposite changes occur when resistance to the infection develops.

As the outcome of these changes in numbers of monocytes and lymphocytes, it is found that the ratio between them increases in proportion with the severity of the invasion and decreases in proportion to improving resistance. In general, this ratio is found to be a very good index of the condition of the patient. We have called this value the "monocyte-lymphocyte ratio."

This is a preliminary report.

While the findings thus enumerated correspond to those reported in the rabbit with generalized tuberculosis, the more chronic type of the disease in the human, and the greater tendency to differences in localization and to the complication by other disease factors, makes the findings in the human more difficult to analysis, and hence requires a greater number of studies before conclusions may be drawn.

[1] Cunningham, R. S., Sabin, F. R., Sugiyama, S., and Kindwall, J. A., *Johns Hopkins Hosp. Bull.*, 1925, xxvii, 231-280.

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Oral Immunization of Rats Against Pneumococcus Types 2 and 3.

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We have previously reported on the successful immunization of white rats against pneumococcus Type 1 by oral administration of the living[1] or acid killed germ.[2] We wished to see whether our results with Type 1 could be duplicated with Types 2 and 3. The organisms were grown on glucose meat extract media but no HCl acid was added to kill the growth. After centrifuging, the germs were mixed with cracker meal and water, and growth from 50 ccm. was fed to each rat daily for 18 to 21 days. Tests were made by injecting intraperitoneally in volume of 0.20 ccm.

When the first feeding experiment with Type 2 was completed it was found that the treated animals tolerated large doses, but that the controls did the same. On reexamining virulence tests which had been made earlier, and, on extending these tests, it was learned that small untreated rats (up to ca. 85 to 95 grammes) were relatively as susceptible (with exceptions) to Type 2 as to Type 1, 10^{-7} and 10^{-6} cc. being fatal doses. However, rats, from this range of weight and above, showed a distinct tendency to rapidly increasing resistance. The age or weight at which this relative immunity begins to develop cannot be given more definitely, since individuals in the same group as well as whole groups of animals vary in this respect. The increased resistance is entirely out of proportion to the increased weight, and at its maximum is of the magnitude obtained to Type 1 when this germ is fed. It may be that the tolerance of the larger animals to Type 2 follows, with changing diet, the ap-