interplay of cultural and environmental forces. Environments are not properly appraised in terms of arithmetic only, such as statistics about soils of ascertained natural fertility, combined with statistics showing seasonal variations of rainfall and temperature. The natural aptitudes of peoples count greatly. Necessity and will also drive men to change their ways and to do the unexpected and even the uneconomic. Migrations still play their vital role. In one country of the Western Hemisphere a foreign element of 260,000 Asiatics, among a group of 6,000,000, now control certain economic activities so largely that their ejection would threaten economic ruin. The causes of such instances require identification. Post-war economic necessities will drive every country to inventory its resources and develop them more intensively, tighten economic administration, and see geographical relations more clearly than ever before. These are the indispensable preliminaries of sound national policies.

# SPECIAL ARTICLES

## SEROLOGICAL REACTIONS WITH AN INDIFFERENT STREPTOCOCCUS IN PRIMARY ATYPICAL PNEUMONIA[1,2,3]

AN indifferent streptococcus (No. 344) was isolated recently from the lung of a fatal case of primary atypical pneumonia. Convalescent sera from patients with this disease were found frequently to possess the capacity to agglutinate this bacterium, while, in most instances, agglutination did not occur with acute-phase sera from the same patients, with the sera of normal individuals or with the convalescent sera of patients with certain other acute infectious diseases. Moreover, convalescent sera from some patients with primary atypical pneumonia yielded precipitates when mixed with soluble substances extracted from this micro-organism, while control sera did not.

Streptococcus 344 was isolated by the inoculation of a suspension of tissue from a human lung into the yolk sacs of chick embryos. It was readily cultivated on blood agar or in beef infusion broth, and grew well under aerobic or anaerobic conditions. On blood agar, small, gray, coniform colonies with slightly serrated surfaces were produced. No hemolysis occurred during 48 hours' incubation on blood agar prepared from rabbit, sheep or human blood. Suspensions of this organism were not soluble in bile. Fermentation reactions, in preliminary tests, did not serve to differentiate this bacterium from other indifferent streptococci.

Bacterial suspensions for agglutination tests were prepared from 24-hour cultures in broth. The bacteria were sedimented, washed three times with saline solution, killed by heating at 56° C. for 30 minutes, and resuspended in saline solution so that the turbidity approximated No. 5 in the McFarland series. Twofold dilutions of unheated serum in saline solution were mixed with equal volumes of the suspension. The final dilutions of serum ranged from 1:10 to 1:160. Tests were not carried out with serum dilutions of less than 1:10, since it was found that the bacterial suspension often agglutinated in 1:2 and occasionally in 1:4 dilutions of normal serum. Following 2 hours at 37° C. and 18 hours at 4° C. the tubes were shaken and readings were made.

Agglutination tests were performed with sera from 101 patients with primary atypical pneumonia. Sera were obtained during the acute phase of the disease and at varying periods in convalescence. Similar tests were made with acute and convalescent sera from patients with acute respiratory infections without pneumonia, psittacosis, pneumococcus pneumonia, influenza A, scarlet fever and other severe streptococcus infections. The sera of 50 normal individuals were also tested.

The results of these tests are shown in Table 1. The convalescent sera of 55 patients with primary atypical pneumonia agglutinated streptococcus 344 at dilutions ranging from 1:10 to 1:160. On the other hand, the acute-phase sera from the same patients did not cause agglutination of this bacterium except in 3 instances, in which positive reactions occurred at 1:10 dilutions. The sera from patients with pneumococcus pneumonia were negative in this test, as were also the sera from patients with psittacosis, scarlet fever and influenza A. The convalescent sera of 2 patients with acute respiratory infections without pneumonia showed titers of 1:10. One patient with Group F minute beta hemolytic streptococcus empyema developed a serum titer of 1:40 and the serum of another patient with subacute bacterial endocarditis caused agglutination at a dilution of 1:80. All the sera from 50 normal individuals failed to produce agglutination under the conditions of this test.

In the majority of instances, positive agglutination

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[2] The Bureau of Medicine and Surgery of the U. S. Navy does not necessarily undertake to endorse views and opinions which are expressed in this paper.

[3] The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and The Rockefeller Institute for Medical Research.

TABLE 1

RESULTS OF AGGLUTINATION TESTS WITH STREPTOCOCCUS 344 AND HUMAN SERA

| Diagnosis | Number of patients | Serum | Agglutination titer of serum | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | <1:10 | 1:10 | 1:20 | 1:40 | 1:80 | 1:160 |
| | | | Number of patients with indicated titer | | | | | |
| Atypical pneumonia ..... | 101 | Acute ..... | 82 | 3 | 0 | 0 | 0 | 0 |
| | | Conval. .... | 46 | 31 | 14 | 4 | 4 | 2 |
| Acute resp. infection ..... | 20 | Acute ..... | 20 | 0 | 0 | 0 | 0 | 0 |
| | | Conval. .... | 18 | 2 | 0 | 0 | 0 | 0 |
| Psittacosis ..... | 4 | Acute ..... | 4 | 0 | 0 | 0 | 0 | 0 |
| | | Conval. .... | 4 | 0 | 0 | 0 | 0 | 0 |
| Pneumococcus pneumonia .. | 28 | Acute ..... | 28 | 0 | 0 | 0 | 0 | 0 |
| | | Conval. ... | 28 | 0 | 0 | 0 | 0 | 0 |
| Influenza A ..... | 12 | Acute ..... | 12 | 0 | 0 | 0 | 0 | 0 |
| | | Conval. .... | 12 | 0 | 0 | 0 | 0 | 0 |
| Scarlet fever* ..... | 10 | Acute ..... | 10 | 0 | 0 | 0 | 0 | 0 |
| | | Conval. .... | 10 | 0 | 0 | 0 | 0 | 0 |
| Streptococcus† infection ... | 2 | Acute ..... | 1 | 0 | 0 | 0 | 0 | 0 |
| | | Conval. .... | 0 | 0 | 0 | 1 | 1 | 0 |
| Normal ..... | 50 | .... | 50 | 0 | 0 | 0 | 0 | 0 |

* Scarlet fever due to Group A hemolytic streptococcus Type XIX.
† 1 patient with subacute bacterial endocarditis. 1 patient with empyema due to group F beta hemolytic streptococcus.

reactions were encountered with sera obtained during the second or third week after the onset of primary atypical pneumonia. Maximum titers were found usually during the third or fourth week, and a sharp diminution in titer frequently occurred during the fifth or sixth week. In many cases the ability of patients' sera to cause agglutination rapidly disappeared, although in some instances agglutination was still caused by sera collected 10 weeks after onset. There appeared to be a positive correlation between the severity of the illness and the development of agglutination reactions with streptococcus 344.

Soluble substances were obtained from concentrated suspensions of the streptococcus by acid extraction at 100° C. and precipitation with alcohol, after which the precipitate was dried and then taken up in saline solution. The procedure was similar to that utilized for the preparation of "M" extracts from beta-hemolytic streptococci.[4] When dilutions of water-clear extracts were mixed in capillary pipettes[5] with convalescent sera from selected patients with primary atypical pneumonia, flocculent precipitates were formed after 2 hours at 37° C. and 24 hours at 4° C. No precipitation occurred with acute-phase sera from the same patients or with normal human sera. Preliminary tests indicate that the results of this test parallel those of the agglutination test but that the precipitin method is less sensitive.

Complement fixation has not been demonstrable with convalescent sera and streptococcus 344, although tests were made with antigens which gave positive reactions in either the precipitation or the agglutination tests.

Convalescent sera which had been heated at 60° C. for thirty minutes were found to have lost almost completely their capacity to agglutinate this bacterium. Heating sera at 56° C. however did not alter the titer. Sera stored at 4° C. for 1 year still gave positive reactions. The bacterial antigen was not impaired by heating at 100° C. for 10 minutes, by 0.5 per cent. phenol, or by storage for 1 month at 4° C.

The results of the streptococcus agglutination tests were found to be correlated in many instances with the results of the cold hemagglutination test[6,7] as well as with the results of the complement-fixation test with mouse lung antigens[8] previously described. However, an appreciable number of convalescent sera were encountered in which only one or two of these tests were positive.

In preliminary experiments the cold hemagglutinin was completely absorbed from a pool of convalescent sera by human red cells without reducing the agglutination titer against streptococcus 344. Conversely, absorption of the pool with this bacterium removed the agglutinin against itself but did not decrease the titer of cold hemagglutinins.

Recently another indifferent streptococcus (No. 9) was isolated from the lung of a second fatal case of primary atypical pneumonia. The results of both agglutination and precipitation tests with this organism were comparable to those observed with streptococcus 344.

Numerous other strains of indifferent streptococci have been isolated which resemble streptococcus 344,

[4] R. C. Lancefield, *Jour. Exp. Med.*, 47: 469, 1928.
[5] H. F. Swift, A. T. Wilson and R. C. Lancefield, *Jour. Exp. Med.*, 78: 127, 1943.
[6] O. L. Peterson, T. H. Ham and M. Finland, SCIENCE, 97: 167, 1943.
[7] J. C. Turner, *Nature*, 151: 419, 1943.
[8] L. Thomas, E. C. Curnen, G. S. Mirick, J. E. Ziegler and F. L. Horsfall, Jr., *Proc. Soc. Exp. Biol. and Med.*, 52: 121, 1943.

morphologically and culturally. These were obtained from the throats or sputa of patients with primary atypical pneumonia, as well as from persons with other acute respiratory infections without pneumonia. As yet, none of these strains has yielded results similar to those obtained with streptococcus 344 in agglutination tests. Agglutination has either failed to occur or has occurred to an equal degree in both acute-phase and convalescent sera. However, when some of these strains were extracted, it was found that soluble substances were obtained which gave results very similar to those observed in precipitation tests with streptococcus 344.

There is as yet no satisfactory explanation for the positive serological reactions which have been observed with streptococcus 344. The available evidence does not warrant the conclusion that this bacterium is a factor in the etiology of primary atypical pneumonia.

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## THE ADRENALS AND SUSCEPTIBILITY TO TRANSPLANTED LEUKEMIA OF RATS

IT was demonstrated some years ago by Jaffe[1] that removal of the adrenals was followed by regeneration of the thymus in old rats and a stimulation of the gland in young rats. A transplantable lymphatic leukemia under investigation in this laboratory has as its most characteristic manifestation an extensive infiltration of the thymus.[2] In the investigation to be reported, the effect of adrenalectomy with its accompanying stimulation of the thymus has been tested on the susceptibility of rats to inoculated leukemia.

Two groups of experiments have been completed. The object of the first was to determine the result of adrenalectomy on the leukemia susceptibility of middle age rats, this being an age when normally the thymus has almost completely atrophied. Even the most receptive strain of rats at this age show a natural resistance, as illustrated by the fact that only 46.9 per cent. of 32 inoculated animals developed the disease. As a contrast to this, rats of the same age and strain subjected to adrenalectomy 15 days before inoculation developed leukemia in 90.3 per cent. of the 31 rats included in the group. The average survival time of the intact rats with the disease was 9.7 day, whereas the adrenalectomized animals averaged only 6.2 day.

In the second group of experiments tests were made of the effect of adrenalectomy on induced resistance of young rats. This state may be brought about by the injection of homologous defibrinated blood two weeks prior to inoculation.[3] In experiments involving 250 rats the following results were recorded. Intact young rats which received the blood injection alone developed leukemia in only 33.9 per cent. of the 59 inoculated. Among the 43 rats adrenalectomized before the injection of defibrinated blood 76.8 per cent. were susceptible and in 42 rats subjected to the reverse procedure, *i.e.*, the blood injection preceding the removal of the adrenals, 92.9 per cent. developed the disease following inoculation. Control rats which received no treatment before inoculation were 96.5 per cent. receptive, and untreated adrenalectomized inoculated rats all died of the disease.

Certain hormones are known to influence malignant conditions in such organs as are normally subject to control by the individual hormone. While in general it is not justifiable to draw conclusions as to the origin of a malignant state from results of a study of transplantation, yet in the present case it may not be amiss to call attention to the fact that the activity of the lymphoid tissue can be influenced by hormones. Therefore it is not unlikely that such hormones play a role in the malignant condition of this tissue, and this likelihood is suggested by the reported results. More direct evidence of this possibility is being accumulated from an extension of the investigation.

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## LOW LIGHT INTENSITY AND COTTON BOLL-SHEDDING

MANY reasons have been given for the shedding of flower buds (squares) and immature bolls by the cotton plant. Aside from insect injury, such factors as drought, fluctuations in soil moisture, impaired fertilization in the flower and load of fruit on the plants have all been shown to be related to the problem of excessive shedding. The studies of Mason[1] in the West Indies and those of Knight[2] in the Sudan, as well as the paper by Canney,[3] suggest that periods of cloudy weather may have considerable effect on the fruiting and shedding of cotton.

In studying the causes of shedding in cotton, recent experiments at the Texas Agricultural Experiment Station indicate that interruptions for two or three days in the high sunlight intensities often causes undue shedding of fruiting forms. For example,

[1] H. L. Jaffe, *Jour. Exper. Med.*, 40: 325–342, 1924; 40: 619–625, 1924; 40: 753–760, 1924.
[2] J. B. Murphy and E. Sturm, *Cancer Research*, 1: 379–383, 1941.
[3] E. Sturm, *Cancer Research*, 1: 627–628, 1941.
[1] T. G. Mason, *Annals Bot.*, 36: 457–484, 1922.
[2] R. L. Knight, *Empire Jour. Exp. Agr.*, 3: 31–40, 1935.
[3] E. E. Canney, *Shirley Inst. Memoirs*, 3: 281–290, 1924.