in its behavior by the cells composing it? Some simple reasons suggest themselves. In the first place, the agent's action to produce a neoplastic change takes place with extreme slowness as compared with the proliferation of the cells, once they have become neoplastic. Consequently the growth of the neoplasm appears to take place entirely by multiplication of the cells of an initial focus. Growth doubtless does take place wholly in this way in many cases because of a second peculiarity of the agent, namely, its dependence on a special set of conditions in order that it may produce a neoplastic change.³ The necessity for such conditions goes far to explain the agent's failure to take an active part in the tumor's dissemination in the body, granting indeed that the agent is present in the circulation before the fowl is moribund. The possibility of immune processes effective against the agent when separate from the cells must be kept in mind. The immune processes thus far recognized have been directed against the cells themselves, as in the case of the mammalian tumors.

The relationship existing between the chicken sarcoma and its cause, as shown by previous papers and by the findings here presented, seems to us to furnish some basis for the conception of an extrinsic cause for other sarcomata.

Sixty-Sixth Street and Avenue A.

BLOOD CULTURES IN PNEUMONIA *

H. W. LYALL, A.B., A.M.

Bacteriologist to Long Island College Hospital

BROOKLYN

That there is a bacteremia in many cases of pneumonia at some time during the course of the disease is now a well-established fact. Just how frequent this condition is, and whether it is actually present in every case are questions which have not been satisfactorily answered. Various observers have published, from time to time, reports of cases with widely varying results. It is possible that these discrepancies may be traced to differences in the technic employed, to the particular time in the course of the disease at which the cultures were taken, or to seasonal or geographic conditions affecting the severity of the disease, dependent, perhaps, on the virulence of the organism.

Rosenow,¹ in this country, and Prochaska,² Silvestrini and Sertoli,³ abroad, report the highest percentage of positive results. Rosenow, in a series of 145 cases, recovered an organism in 132, or 91 per cent. He used, principally, broth in flasks, in which the proportion of blood present represented a dilution of 1 in 50 or 1 in 75. Prochaska, in two series of thirty and ten cases, respectively, reports finding the organism in 100 per cent. This author used both broth and agar, but obtained by far the more satisfactory results with the liquid medium, and points out the advantage of using a high dilution. Silvestrini and Sertoli obtained positive results in fifteen out of sixteen cases, almost all of which ended fatally.

On the other hand, there are numerous other observers whose percentage of positive cultures has been much

lower. Sittman⁴ reports six positive out of sixteen cases, Kuhnau⁵ one out of nine, White⁶ three out of nineteen. Schottmüller,⁷ in a series of 209 cases, found an organism in the circulating blood in only 23 per cent. He used, for the most part, cultures on solid media making several plates representing varying dilutions of blood. Cole,⁸ in 1902, out of thirty cases reported only 30 per cent. positive cultures, using broth and milk. Strouse and Clough,⁹ in one of the most recent papers, obtained positive results in 56 per cent. of cases in a series of twenty-five.

With reference to the recovery of the pneumococcus from the blood at the time of crisis, of lysis or after, results have been more uniform, the majority of authors failing to obtain growth at this time. Rosenow notes positive results after crisis in a few cases, usually when taken a few hours after the onset, although he was successful in recovering the organism as late as six days following crisis in a case of apparently delayed resolution. Wolf¹⁰ reports similar results, obtaining positive cultures after crisis or lysis in six out of fifteen cases. In three of his cases there was delayed resolution, but in the other three there were no clinical complications.

The present series consists of the cases coming under my observation during the season 1911-1912 in the routine bacteriologic work at the Long Island College Hospital. Only those cases which at the time of culture or subsequently could be definitely diagnosed clinically as pneumonia are included in this report. Cases were unilateral lobar pneumonia unless otherwise noted.

TECHNIC

The patient's arm was cleansed, and disinfected at the elbow as follows: The surface was shaved, scrubbed with green soap and sterile water, followed by bichlorid of mercury, alcohol and ether. Preparation was done, preferably, at least an hour before the time for taking the culture and the arm wrapped with a sterile bichlorid compress in the meantime. A Bier's bandage was wound around the arm above the elbow, sufficiently tight to produce a moderate venous stasis, and a small cut made through the skin directly over and parallel with the median cephalic or basilic vein. In making the incision the skin was drawn to one side to avoid the possibility of cutting into the vein. A Luer all-glass syringe of 15 c.c. capacity was used and a Number 18 or 19 needle. The needle was plunged into the vein in the direction of the blood-current. Ten c.c. or more of blood were withdrawn and immediately transferred to a tube containing an equal volume of Epstein's¹¹ ammonium oxalate solution and shaken to prevent clotting. This was taken to the laboratory and the mixture of blood and oxalate planted in suitable media for observation.

MEDIA

All media used, whether solid or liquid, were neutral to phenolphthalein, which, apparently is the

* From the Department of Bacteriology, Hoagland Laboratory.
1. Rosenow: Studies in Pneumonia and Pneumococcus Infections, *Jour. Infect. Dis.*, 1904, I, 280.

2. Prochaska: Bacteriologische Blutuntersuchungen bei Pneumonen, *Zentralbl. f. inn. Med.*, 1900, xxi, 1145.

3. Silvestrini and Sertoli: Sulla presenza del diplococco di Fraenkel nel sangue circolante degli pneumonici, *Riforma Med.*, 1899, II, 483.

4. Sittman: Bacterioskopische Blutuntersuchungen, *Deutsche Arch. f. klin. Med.*, 1894, III, 323.

5. Kuhnau: Ueber die Resultate und die Leistungsfähigkeit der bacteriologischen Blutuntersuchung im Dienste der klinischen Diagnostik, *Ztschr. f. Hyg. u. Infektionskrankh.*, 1897, xxv, 492.

6. White: Blood Cultures in Septicemia and Other Diseases, *Jour. Exper. Med.*, 1899, IV, 26.

7. Schottmüller: Zur Aetiologie der Pneumonia crouposa, *München. med. Wehnschr.*, 1905, III, 1425.

8. Cole: Blood Cultures in Pneumonia, *Bull. Johns Hopkins Hosp.*, 1902, xiii, 135, 136.

9. Strouse and Clough: Blood Cultures in Pneumonia, *Bull. Johns Hopkins Hosp.*, 1910, xxi, 233, 235.

10. Wolf: Latent Pneumococcemia, *Jour. Infect. Dis.*, 1906, III, 446. For more complete bibliography see Rosenow, Wolf and Strouse and Clough.

11. Epstein: Hiss and Zinsser's Text-Book of Bacteriology, p. 176.

optimum reaction for the growth of pneumococci and streptococci. All liquid media contained a small piece of calcium carbonate (as recommended by Hiss¹²) in order to neutralize any free acid formed and thus prevent any acid inhibition of growth. For plating, plain and 1 per cent. dextrose agar were used and plain ascitic, dextrose ascitic and dextrose broth without the addition

TABLE SHOWING RESULTS OBTAINED IN A SERIES OF 45 CULTURES MADE FROM THE BLOOD OF 42 PATIENTS SUFFERING FROM PNEUMONIA *

Culture No.	Day of Disease	Result of Culture	Recovery	Inulin	Bile	Remarks
1	12	0	+	..	..	Double pneumonia, less than twenty-four hours before lysis.
2	12	0	+	..	..	
3	3	+	0	..	..	
4	7	0	+	..	..	
5	5	0	+	..	..	Culture taken after crisis had begun; double pneumonia.
6	6	0	+	..	..	After beginning of crisis. Very mild case. After beginning of crisis; second culture, eighteen hours later, also negative. After beginning of crisis.
7	7	0	+	..	..	
8	4	0	+	..	..	
9	7	0	+	..	..	
10	4	0	+	..	..	100 colonies per c.c. of blood; ½ c.c. of 24-hour culture killed mouse in 18 hrs.
11	5	+	0	..	..	
12	2	0	+	..	..	
13	7	0	+	..	..	
14	2	0	+	..	..	Case 12 at crisis. Very mild.
15	6	+	+	..	..	Crisis four days after culture.
16	2	+	0	+	..	Culture five days before death; typhoid suspected; patient delirious.
17	7	0	+	..	..	After crisis had begun, very mild case.
18	2	0	+	..	..	Twenty-four hours before crisis.
19	5	0	+	..	..	At time of crisis.
20	5	+	+	0	0	Streptococcus; clouding of ascitic-dextrose-agar; 2 c.c. failed to kill rabbit; suspected tuberculosis.
21	5	0	+	..	..	Mild case, central.
22	10	+	+	+	+	Typhoid suspected; long chains in original culture, subsequently lost (2 c.c. killed rabbit in 18 hours; encapsulated diplococci at autopsy).
23	4	0	+	..	..	Twenty-four hours before crisis, mild case.
24	2	0	+	..	..	After crisis had begun.
25	10	0	+	..	..	During crisis.
26	5	0	+	..	..	Just previous to beginning of crisis.
27	5	0	+	..	..	At time of crisis.
28	3	+	+	+	+	Delirium tremens. Subsequent culture positive. Case 32. Patient seven months pregnant. Complicated by pregnancy; patient had apparent crisis but developed pneumonia of other lung.
29	5	+	+	+	+	
30	5	0	0	..	..	
31	5	0	0	..	..	
32	4	0	0	..	..	Clouding in dextrose-ascitic-agar.
33	3	+	0	+	+	Clouding in dextrose-ascitic-agar; hemolysis marked.
34	8	+	0	+	+	Patient developed delirium tremens.
35	3	+	0	+	+	Patient developed delirium tremens.
36	10	+	0	0	0	Subsequent culture.
37	3	+	0	+	+	
38	1	+	0	+	+	
39	4	0	+	..	..	
40	5	+	0	+	+	Died after apparent crisis; delirium tremens.
41	3	0	+	..	..	
42	10	+	+	+	+	
43	7	+	0	+	+	
44	5	0	+	..	..	Case 41. Two days before lysis set in.
45	4	0	+	..	..	Slight involvement upper lobe.

* Number of cases, 42; positive, 17; percentage of positive cases, 40.5 per cent.; number of cultures taken during crisis or lysis, 10; deducting cultures taken during crisis or lysis, percentage of positive cultures, 53 per cent.; total death-rate, 26.2 per cent.; death-rate in positive cases, 53 per cent.; in negative cases, 8 per cent.
† Eighteen hours.

of any enriching fluid were used for flask cultures. The flasks contained from 150 to 200 c.c. of broth and therefore represented a dilution of the blood of from 1 in 20 to 1 in 50, according to the amount of blood used. The medium which gave the best results was the dextrose-calcium-carbonate broth without the addition of any

enriching fluid. Apparently the amount of blood added furnishes enough enrichment to allow the pneumococcus to grow abundantly without exerting any inhibiting effect. The advantage in the use of liquid media over the plate method was marked. In almost every case in which the broth cultures were positive the plates failed to show any growth. This occurred in several cases in which a profuse growth was obtained in broth in from twelve to twenty-four hours. The most reasonable explanation seems to be that the higher dilution present in the broth culture allows better diffusion and consequent dilution of the bactericidal or other inhibiting substances present in the blood.

Ordinarily, growth was apparent within twenty-four hours, as indicated by a clouding of the medium and a change in the color of the blood. This varied from a slight discoloration to a brownish-black. Hanging-drop and stained preparations were made in order to observe morphology, and subcultures made on hydrocele-agar and calcium-carbonate-hydrocele broth to facilitate study of the colonies and chain-formation. The organisms obtained were then identified by means of the inulin, bile and hemolytic tests. A few strains were tested for virulence by inoculation into rabbits. The appearance of the growth in dextrose-hydrocele-agar was also instructive when there was the possibility that the organism in question might be a streptococcus. The streptococci invariably produce a distinct clouding of this medium, whereas no change is noticed in the case of the pneumococci.

The accompanying table shows the results obtained in the series of forty-five cultures.

Although it is not to be expected that any definite conclusions can be drawn from the above table, representing, as it does, such a small number of cases, yet some points may be emphasized. It is apparent that we are not dealing with a series in which the total death-rate is high, as compared with some of those reported. Of the seventeen positive cases, one-half of that number of patients died, so that it would appear that the finding of organisms in the blood is not absolute as far as its prognostic value is concerned. The fact that of the negative cases only three patients died might seem to indicate that positive findings bear some relation to the severity of the disease. In ten cultures taken at the time of or during crisis or lysis, uniformly negative results were obtained; in no case was any organism recovered from the blood. Just what the relation is between crisis and the disappearance of the organism from the blood, whether it is dependent on the accumulation of antibacterial substances which influence the viability of the organism when transferred to artificial media, or on other factors, the mechanism of which we do not fully understand at present, cannot be definitely stated.

In cases in which positive results were obtained it is hard to see wherein the time at which the culture was taken, in relation to the progress of the disease, had any influence. In one case in which the exact time and nature of the chill could be observed, owing to the fact that the patient developed the disease while in the hospital, the culture taken eighteen hours after the initial chill remained sterile, whereas one taken two days later showed an abundant growth of pneumococci. It is to be regretted that more subsequent cultures were not taken. The above is the only one in which a second culture was positive where the first was sterile. The three other cases in which a subsequent culture was taken gave negative results each time.

It is of interest to note that in three cases organisms were isolated which, by all differential tests, would be classed as streptococci. None of these organisms fermented inulin or were dissolved by bile. All produced a clouding in dextrose-ascitic agar. Two were non-pathogenic for rabbits in doses of 2 c.c. of a twenty-four-hour broth culture, a dose which is invariably fatal with pneumococci.

As to the value of blood cultures as an aid to diagnosis, the field appears to be rather limited. As a rule, the clinical symptoms are sufficient to warrant a positive diagnosis. In three cases of the above series, the blood culture was of distinct advantage in the differential diagnosis, in two suspected cases of typhoid fever, and in one of suspected miliary tuberculosis.

SUMMARY

The points which seem to be of greatest interest, are:

1. In this series, characterized by a low total death-rate, blood cultures were positive in only 40 per cent.

2. The total number of cases was forty-two, of which seventeen, or 40.5 per cent., were positive, and twenty-five, or 59.5 per cent., were negative. The total mortality was eleven, or 26.19 per cent.; five patients who died were alcoholics. The positive cases showed a mortality of eight, 53.5 per cent., among which were four alcoholics. The negative cases showed a mortality of three, 8 per cent.; one patient who died was an alcoholic. On account of the incidence of alcoholism, it is difficult to draw any definite conclusions as to the relation between positive findings and prognosis.

3. All cases at the time of, or after, crisis or lysis gave uniformly negative results.

4. Calcium-carbonate broth seems to furnish a most suitable medium for the growth of pneumococci and streptococci and possesses an additional advantage over solid mediums of securing a sufficiently high dilution of the blood.

5. In three cases organisms which are to be classed as streptococci were obtained in pure culture. These did not show any of the characteristics of *Streptococcus mucosus capsulatus*.

I desire to express my sincere thanks and appreciation for the hearty cooperation shown by the visiting and house staffs at the Long Island College Hospital.

AN ESSAY OF HEALTH AND LONG LIFE, PUBLISHED A. D. 1725 *

WILLIAM H. CRISP, M.D.
DENVER

The science of medicine may be considered as just passing from infancy into childhood. The art of medicine is a trifle older. The fond relatives of the former young gentleman, who is only beginning to feel steady on his legs, are already disposed to look condescendingly down on the other youth, who had his birthday back in those dark ages before the dawn of human civilization, and has been growing very slowly, but very steadily, ever since. The study of history develops a sense of perspective, which in its turn encourages tolerance, breadth of view and hope of future growth. In such a society as this it would surely be both interesting and profitable if we could now and then turn aside from

regarding the deeds of the present and give a little time to the study of those of the past.

The leading physicians of the seventeenth and eighteenth centuries devoted a good deal of energy to an attempt to construct complete theoretical systems on which to base all their understanding and treatment of the human body and its ailments. In the light of the modern accumulation of accurate scientific observations, these dead systems often furnish much amusement to those who read them; and their foundations and conclusions are often equally ludicrous. Fortunately there were also brilliant practitioners and students who, like Sydenham, saw and taught that one may profitably study individual processes and organs without making the facts acquired fit in with any preconceived hypothesis. This attitude is well presented in the following passage from a letter by John Locke, physician and philosopher, to W. Molyneux:

"You cannot imagine how far a little observation carefully made by a man not tied up in the four humours, or sal, sulphur, and mercury, or to acid and alkali, which has of late prevailed, will carry a man in the curing of diseases though very stubborn and dangerous; and that with very little and common things, and almost no medicine at all."

It seems that our so-called therapeutic nihilists are not the first of their kind.

George Cheyne, with one of whose writings this paper will deal, was born in Aberdeenshire, Scotland, in 1671, the year in which Isaac Newton published his "Theory of Light." He died at Bath, England, in 1743. In his earlier years he was a follower of the iatromechanical school, so named because it attempted to explain all disease processes on a mechanical basis. He tells us that the first time he adventured in print was in a work on the theory of fevers, which he completed in a few days, and which was done in defense of his "great master and generous friend" Dr. Pitcairn. This was at the age of 31. He later sallied into a "book of abstracted geometry and algebra," entitled "Methodus Fluxionum Inversa." When 54 years old, or in 1725, he issued the fourth edition of the work with which this paper is more directly concerned, "An Essay of Health and Long Life." The date of the first edition I have not ascertained. The book is a curious mingling of abstract hypothesis with the common-sense results of a life of practical experience. It is dedicated to Sir Joseph Jekyll, Master of the Rolls, one of Cheyne's patients for whom it was originally written, and at whose request, says Cheyne, it was given to the public. It is an octavo volume of 232 pages, plus twenty pages of preface and a table of contents of the same length.

As regards the literary style and historical associations of the book, it is interesting to recall that Defoe's "Robinson Crusoe" was published in 1719, and Jonathan Swift's "Gulliver's Travels" in 1726; and that Cheyne was contemporary with the poet Pope, whose classic translation or English version of Homer's "Odyssey" was issued between 1723 and 1725. In the year of publication of this fourth edition of Cheyne's essay, Samuel Johnson was a mere youth of 16 years, and his famous dictionary first saw the light twenty years later. David Hume's charming but inexact history of England, and the foundation of the modern novel in the stories of Richardson, Fielding, Smollett and Sterne did not appear until from 15 to 35 years later. It was about 100 years since, in the dissecting-room and through the printing press, that William Harvey first taught his theory of the circulation.

* Read before the Medical Society of the City and County of Denver, March 10, 1912.