drawn up to the 0.4 cc. mark. A small air bubble, about .01 cc. or less, is also drawn in, which is important for stirring and mixing the 2 solutions. This is accomplished by inverting the tube 6 or 8 times. Liquid junction is made to a saturated calomel cell by clamping the tube upright in a beaker containing saturated KCl. The potential is measured at 30 seconds, and again at 40, 50, and 60 seconds. The drift in potential between 30 and 60 seconds is usually 2 millivolts, and it is assumed that the drift between zero time and 30 seconds would have been one millivolt greater, or 3 millivolts. The calculation is best illustrated by a particular case. If the observed potentials at 30 and 60 seconds are +9 and +11 millivolts, respectively, then it is assumed that at zero time the potential is +9—3 or +6 millivolts. From the conventional constants for quinhydrone at 25°, (saturated calomel), $pH = \frac{.453 - E \text{ observed}}{.059}$. This gives a $pH = 7.58$ at 25°. Assuming a change in pH with change in temperature of —.012 pH per degree, this would become $7.58 - (13.0 \times 0.012 = 7.58 - 0.16 = 7.42$ at 38°.

By using equal volumes of serum and saturated quinhydrone solutions, uniformity in the speed of formation and in the concentration of the quinhydrone solution are insured, and thus a uniform drift in potential is obtained. The drift is less rapid than if serum is saturated with quinhydrone, as Wilson[2] has pointed out, while the pH of the serum is not appreciably altered by this dilution.

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Production of Experimental Lobar Pneumonia in the Dog.*

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Until the work of Cecil and Blake[1] lobar pneumonia had not been produced constantly and successfully in the lower animals. These authors employed the *Macacus syrichtus,* a Philippine monkey which is apparently more susceptible to the pneumococcus than the other varieties. Their method consisted simply of intra-

* This work has been conducted under a grant from the Douglas Smith Foundation for Medical Research of the University of Chicago.

[1] Blake, F. G., and Cecil, R. L., *J. Exp. Med.*, 1920, xxxi, 403.

tracheal injections of small quantities of pneumococci. The disease produced and the lesions observed corresponded closely with lobar pneumonia in man. However, the subsequent employment of this method with other species has failed to produce lobar pneumonia apparently because they were more resistant to the pneumococcus than the *Macacus syrichtus* which unfortunately is no longer allowed to be imported into the United States. Others working with the dog have found that in order to produce pulmonary infection with the pneumococcus, not only must the infecting agent be implanted far down in the bronchial tree but the inoculum must be massive. Lamar and Meltzer[2] using this method were successful in producing in some of their animals lobar consolidation and a disease resembling an abortive lobar pneumonia. But the infected animals which lived longer, died within 2 to 4 days with bacteremia and pyemic complications without true consolidation of the lung. Many of their dogs escaped infection. More recently Coryllos and Birnbaum[3] have employed a modification of this method, spraying large quantities of pneumococci culture into the lung through a bronchoscope either with or without subsequent occlusion of the main bronchus. This resulted either in a transient infection or a widespread pneumonia accompanied by atelectasis with an ensuing generalized infection and fatal termination.

Thus the methods previously used in an attempt to produce lobar pneumonia in dogs, not only have failed to induce the characteristics of the disease as seen in humans, but have employed a dosage which is enormously greater than could occur in the spontaneous inception of the disease in man. The results of previous investigation into the state of the circulating antipneumococcus resistance at the time of the onset of the disease[4] led us to infer that the pneumococcus begins its initial growth in the lungs protected from the pneumococcidal action of the blood which in both dogs and humans is considerable. It seemed probable that if pneumococci were implanted in the lungs in a medium which would allow them to grow protected from the pneumococcus killing properties of the blood, the disease might be initiated with relatively small numbers of organisms. In other words, it might be possible to initiate in a general way conditions giving rise to the spontaneous occurrence of lobar pneumonia in man.

After attempting different means we have adopted a method

[2] Lamar, R. V., and Meltzer, S. J., *J. Exp. Med.*, 1912, xv, 133.

[3] Coryloss, P. N., and Birnbaum, G. L., *Arch. Surg.*, 1929, xviii, 190.

[4] Robertson, O. H., Terrell, E. E., Graeser, J. G., and Cornwell, M. A., in press.

which consists in the intrabronchial injection of 0.05 cc. to 0.5 cc. of an 18 hour culture of Pneumococcus Types I or II, suspended in a viscous starch-broth mixture. For this purpose a radio-opaque catheter is inserted under the fluoroscope and 0.5 cc. to 1 cc. of this pneumococcus starch suspension instilled into a small bronchus as near the periphery of the lung as possible. As a rule, within 24 hours typical lobar consolidation of the injected lobe has occurred as evidenced by x-ray and physical findings. The disease runs a febrile course of 3 to 7 days; the pneumonic lesion either remains localized in one lobe or spreads from lobe to lobe. This experimental disease resembles the natural disease in humans in the manner of the spread of the lesion, the localization of the process (pneumococci do not usually invade the blood stream), the immune response, the abrupt termination of the disease by crisis, lysis, or death and the rapid regression of the process after recovery. Animals were killed at different stages during the disease from one hour after injection of the infecting dose to one or 2 days following recovery. The lesion was found to spread evenly and contiguously thru the lobe, the line of the advancing process usually being sharply demarcated from the normal tissue. With the evolution of the disease the lesion progressed through the different stages observed in the human pneumonic lung from an initial marked congestion to red hepatization and finally to a modified gray hepatization. The microscopic pathology was that of a lobar pneumonia from the beginning and in its general characteristics resembled the picture of the human disease. Certain differences from the human pneumonic lungs were observed. These were the greater degree of blood vessel engorgement seen all thru the disease, the smaller amount of fibrin, and the more rapid decrease in size of the resolving lung.

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On the Production of Variant Colonies by Certain of the Intestinal Bacteria.

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Much of the literature on microbic dissociation has emphasized the occurrence of rough (R) colonies, in contrast to the smooth (S) form, with, on the whole, relatively little mention of other