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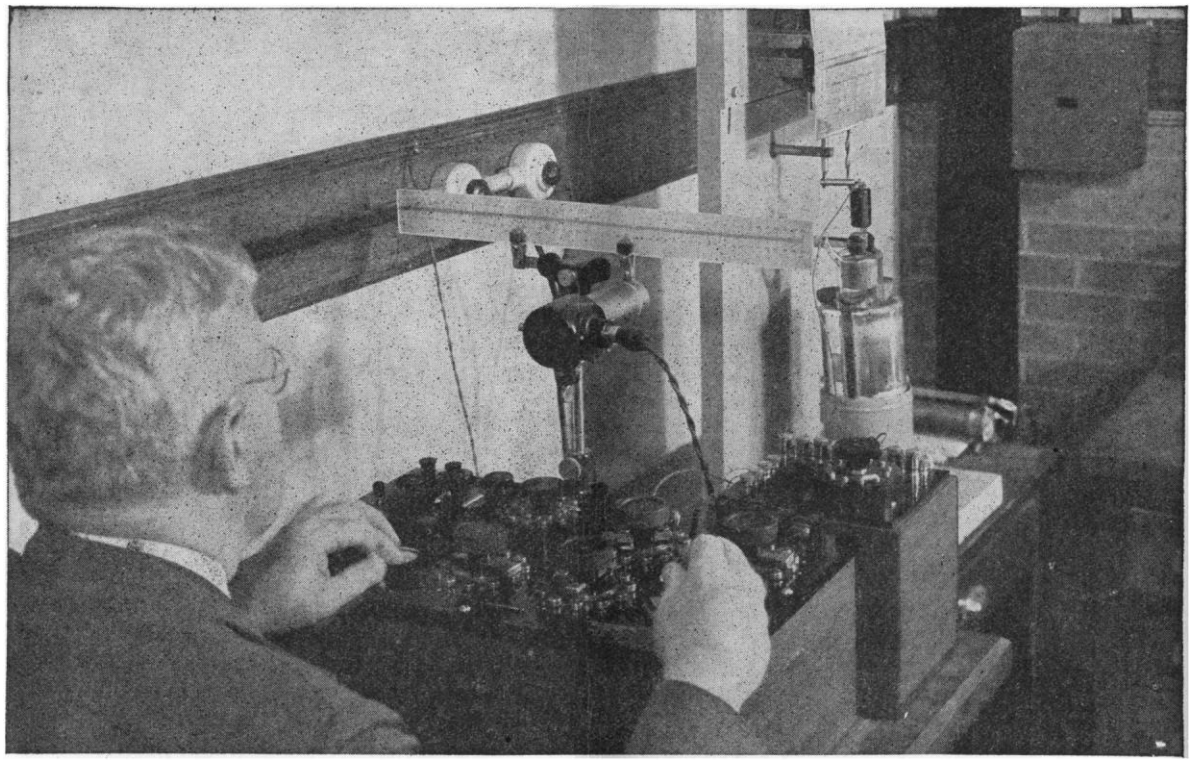

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PATHWAYS OF MEDICAL PROGRESS[1]

By Dr. CARL J. WIGGERS

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ON occasions such as this we gather together from laboratories and hospitals as disciples of scientific medicine. We assemble, primarily, for the purpose of exchanging views on problems which seem to have crystallized for each of us individually. Current reviews thus prepared by thoughtful minds and representing diverse perspectives afford those engaged in other fields an opportunity to keep in touch with the trends of contemporaneous research in specialized fields.

But these occasions have other functions, too. The frank exchange of opinions and the exposition of facts upon which they are founded serve to re-energize us, even if like opposite charges they outwardly seem to repel. As no effective electrical forces can exist without positive and negative charges, so no dynamic forces can be induced in research without a polarity of opinion. Furthermore, we who, despite earnest efforts, frequently become dissatisfied with our own contributions need to revitalize our faith occasionally by noting that the summation of modest efforts has contributed quite as much to medical progress as the occasional big discoveries.

However, impressive as the advance has been during the past quarter century, occasions such as this are opportune for reexamining our current methods and procedures with a view to planning still more efficient and economical means for accelerating it. I shall attempt to review the major pathways over which we have reached our present state of progress in medicine, and, as we proceed, shall stop occasionally to note the ruts in the road and obvious suggestions for their repair. Since this assembly is dominantly interested

[1] Address of the vice-president and chairman of the Section on Medical Sciences, American Association for the Advancement of Science, Columbus, December 28, 1939.

were enlarged for greater quantity production by one of the writers with Macchiavello.[12] While immunologically valid and quantitatively more useful than the Weigl method, the Maitland technique still remains inadequate for large-scale work.

Recently, two further techniques have been described. The first of these is our own agar tissue procedure which, now adapted to use with Kolle flasks, furnishes considerable amounts of vaccine;[13,14] the second is the Cox method of inoculation of fertile hen's eggs.[15] In 1934[16] Dr. Zia demonstrated in our laboratory that European and murine Rickettsiae would grow on the chorio-allantoic membranes of hen's eggs, but the yield was too small for practical purposes. Cox inoculated directly into the yolk sac. Microscopically, he finds few if any Rickettsiae of various types in the chorio-allantois and in tissues of the embryo itself. In the yolk sacs, however, Rickettsiae are numerous with the spotted fever and murine typhus infections, though none were found in the European variety of typhus.

We have repeated the Cox method, using the European strain, and have passed the virus to date through 15 egg passages. The embryos die regularly after 4 days. After several passages, we begin to find Rickettsae in the yolk membranes, although they are rarely very numerous. We have never found Rickettsiae in the embryos themselves. Comparisons between the egg method and our own agar technique indicated that, as far as yield of active material was concerned, the two procedures were of the same order, although the yolk membranes of the eggs infected with the European virus titrated somewhat higher in guinea pigs than did the material from the agar tubes—in the proportion of about 10^{-7} to 10^{-6}. There are, however, some advantages in the agar method, such as greater ease of cellular elements from the vaccine and more accurate morphological control.

The method which we now employ to secure large numbers of Rickettsiae consists in a combination of the agar method—using considerably enlarged surfaces for cultivation—and the egg technique as a source of inoculum. Specifically, the minced embryonic tissue or macerated yolk sac taken from eggs on the fourth day following infection is used to inoculate large quantities of normal minced chick tissue from 10-day embryos. The tissue thus infected is distributed in large amounts on the agar surfaces of modified Kolle flasks. The neck of the ordinary flask is replaced by one which will receive a No. 6 rubber stopper. After 6 or 7 days' incubation at 37° C., cultures very rich in Rickettsiae are obtained. We emphasize the fact that considerable quantities of tissue may be employed. Transplants can then be made by using the culture Rickettsiae or new cultures inaugurated with material from infected eggs.

By this method, with a personnel of one bacteriologist and two technicians, one liter of vaccine sufficient for 300 complete immunizations can be produced in a week. Increase of production is only a matter of enlarging equipment and personnel.

Since embryonic mouse tissue has also been used successfully in the agar method, it could be substituted for the chick material. For the present, however, the latter gives excellent yields and has proved satisfactory.

HANS ZINSSER
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BOOKS RECEIVED

Academy of Political Science, Proceedings. *Vol. 18, No. 4. The Effect of the War on America's Idle Men and Idle Money.* JOHN A. KROUT, Editor. Pp. x + 133. The Academy, Columbia University.

CUTRIGHT, PAUL R. *The Great Naturalists Explore South America.* Pp. xii + 340. Illustrated. Macmillan. $3.50.

FIELD, HENRY. *Contributions to the Anthropology of Iran; Anthropological Series: Vol. 29, No. 1.* Pp. 507. 20 figures. $5.50. *No. 2.* Pp. 511–706. 4 figures. 144 plates. $2.25. Field Museum.

HAGUE, B. *An Introduction to Vector Analysis for Physicists and Engineers.* Pp. viii + 118. 39 figures. Chemical Publishing Co. $1.50.

Harvard Meteorological Studies: No. 3, Pressure and Temperature Variations in the Free Atmosphere Over Boston. B. HAURWITZ and E. HAURWITZ. Pp. 74. 23 figures. $0.90. *No. 4.* STERLING P. FERGUSSON. *Experimental Studies of Anemometers.* Pp. 101. 39 figures. $0.90. Harvard University Press.

LEA, C. H. *Rancidity in Edible Fats.* Pp. vi + 230. 38 figures. Chemical Publishing Co. $4.00.

MORANT, G. M. and B. L. WELCH. *A Bibliography of the Statistical and Other Writings of Karl Pearson.* Pp. 119. *Biometrika*, University College, London.

NICOL, HUGH. *Plant Growth-Substances; Their Chemistry and Applications, with Special Reference to Synthetics.* Pp. xii + 106. 6 figures. Chemical Publishing Co. $2.00.

SHOHL, ALFRED T. *Mineral Metabolism.* Pp. x + 384. 13 figures. Reinhold. $5.00.

STRONG, REUBEN M. *A Bibliography of Birds; Zoological Series, Vol. 25: Part 1.* Pp. 464. $6.00. *Part 2.* Pp. 469–937. $6.00. Field Museum.

Symposium on the Blood and Blood-forming Organs. Addresses Given at an Institute Conducted by the Medical School of the University of Wisconsin, September 4–6, 1939. Pp. viii + 264. Illustrated. The University Press. $3.50.

TORY, H. M., Editor. *A History of Science in Canada.* Pp. vi + 152. Illustrated. Ryerson Press, Toronto. $2.50.