mum weight of dry bacilli, 1.37 g per 100 cc of culture medium, was obtained at about this time. Thereafter the weight of organisms steadily diminished, due to rapid autolysis. The point at which autolysis was first noted corresponds with the time at which considerable quantities of tuberculin are usually found in the medium.

Quantitative determinations of lactic acid[8] failed to reveal even traces in any of the cultures.

Conclusions. It is shown (1) that the rapid growth of the microorganisms is directly related to the consumption of glycerol and other constituents of the synthetic medium, and (2) that rapid autolysis occurs after exhaustion of the nutrients.

10793 P

Capillary Permeability in the Skin of the Rabbit.*

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The mechanism by which capillaries permit dyes and particulate matter to escape in increased amounts is not clearly understood. Many investigators have observed certain physiological and pathological changes in experimental animals in which the capillaries were more permeable than normal. Burrows[1] and Menkin[2] have stated that trypan blue and India ink when injected intravenously localize and concentrate in areas of inflammation. The latter has also shown that such substances when injected into areas of inflammation are retained longer than when they are injected into normal tissue.

Recent studies in this laboratory have shown that trypan blue and India ink do not always concentrate in areas of inflammation produced by the local application of xylol in the skin of rabbits. These substances concentrate in such areas only when they are injected into the circulation immediately or within a period of less than 5 hours following the application of the xylol. The fact that trypan blue and carbon particles fail to concentrate in xylol-treated areas

8 Friedemann, T. E., and Graeser, J. G., *J. Biol. Chem.*, 1933, **100**, 291.

* Aided by grant from the Division of Medical Sciences, Rockefeller Foundation.

1 Burrows, H., *Localization of Disease*, Wm. Wood and Co., 1932, New York.

2 Menkin, V., *Physiol. Rev.*, 1938, **18**, 366.

of skin is very interesting since these areas of skin after 5 hours show all the macroscopic and microscopic changes associated with inflammation.

The rabbits were carefully shaven 24 hours or longer before they were used in these experiments. Areas of skin on the sides of these animals were outlined in India ink. Xylol was carefully applied to these areas with a cotton swab. Care was taken not to massage the skin during the application of the irritant. Frequently the xylol diffused along the surface of the epithelium outside the areas marked out with the ink. The skin became blanched immediately following the application of xylol and within a period of less than a minute thereafter it became hyperemic. The areas apparently became edematous within 10 minutes following the application of the irritant. Following an intravenous injection of trypan blue in a 0.2% saline solution the dye localized in the area of skin where xylol was last applied, usually within an interval of 5 minutes or less. The amount of dye that localized in the xylol-treated areas of skin decreased with an increase in the interval between the application of the irritant and the injection of the dye during a period of approximately 2 hours. After this time essentially the same quantity of trypan blue localized in the treated and untreated areas of skin.

Dr. Ralph D. Cressman and I recently observed that rabbits anesthetized with either alcohol or ether failed to show a localization of trypan blue in areas of skin treated with xylol within the same time as the normal animals. The dye appeared first in the areas of skin treated with xylol 15 minutes before the dye was injected rather than in the last areas as observed in the normals. The time that trypan blue first appeared in the xylol-treated areas of skin in the normal rabbits did not occur in every animal as described above, however, the variation in the anesthetized and non-anesthetized rabbits did occur in a sufficient number of animals apparently to be significant.

Staphylococcus antitoxin, diphtheria antitoxin and a saline suspension of vaccine virus each have been found to localize in areas of inflammation produced by xylol when given intravenously immediately following the application of the irritant. There is no concentration of either the antitoxin or the virus in the areas of irritation if they are injected intravenously 24 hours following the application of the xylol.

The observation that capillaries show an increase in permeability for antitoxin is significant from a therapeutic standpoint. Medicinal

preparations given intravenously may be concentrated in the tissue by increasing the capillary permeability through the use of counter irritants. Neoprontosil has been observed to localize and concentrate in areas of the rabbits' skin when it was given intravenously immediately following the local application of xylol. A complete study will subsequently be made on the localization of blood-borne materials in areas of inflammation.

The indications are from my observations that increased capillary permeability is of brief duration following injury where xylol is applied and apparently is a phenomenon distinct from that by which leucocytes reach the area of inflammation. The two phenomena however frequently occur together.

The results obtained in these experiments on the relation between the time of application of xylol to the skin of rabbits and the time of localization and concentration of trypan blue following an intravenous injection are similar to the observations of Kline and Winternitz.[3] The latter investigators found that when pneumonia was produced in rabbits with vital stain in their circulation, the involved lung had a uniform blue color; if, however, the dye was injected sometime after the pneumonia developed (20-65 hours) pale gray consolidated areas occurred in the otherwise densely blue stained pneumonic lobes.

10794 P

In vitro Incorporation of Fatty Acids in Phospholipids of Intestinal Mucosa.*

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Sinclair,[1] using elaidic acid, found that phospholipids of the intestinal mucosa after feeding fat, contained some of that fed fat. Perlman, Rubin, and Chaikoff[2] later showed that fed, radioactive phosphorus also became incorporated in the phospholipids of the

3 Kline, B. S., and Winternitz, M. C., *J. Exp. Med.*, 1915, **21**, 311.

* Aided by grants from the Rockefeller Foundation and the National Live Stock and Meat Board.

1 Sinclair, R. G., *J. Biol. Chem.*, 1929, **82**, 117.

2 Perlman, I., Rubin, S., and Chaikoff, I. L., *J. Biol. Chem.*, 1937, **122**, 169.