stant, and was 5 times higher than in dog plasma.

These differences in results are probably traceable, at least in part, to technical factors of the methods. It appears that the procedure employed in this study is more sensitive and perhaps subject to less error. Nevertheless, when the two methods are applied to normal plasmas they yield results which roughly parallel each other, and both show a low concentration of labile factor in human blood. More important but far more difficult to harmonize and discuss critically are the differences in views concerning the action of the labile factor. Owren, Fantl and Seegers look upon this factor as an accelerator or catalyst, while the writers conclude that it reacts stoechiometrically since a manifold increase in its concentration does not alter the prothrombin time nor the speed of prothrombin conversion.[10] Recently findings have been made which clearly suggest that prothrombin in human blood exists partly in an active form and partly in a precursor state.[11] This discovery introduces a new element in the clotting mechanism requiring evaluation. It is likely that the concept that prothrombin *per se* can change its convertibility or that catalysts can alter it, will require reinterpretation. Since the one-stage method measures active prothrombin, and the two-stage probably total prothrombin, findings such as those reported by Owen and Bollman[12] that the two methods when applied to dicumarolized blood showed marked difference in prothrombin level can be explained without postulating a factor which changes the rate of conversion of prothrombin to thrombin.

Conclusions. The labile factor of the prothrombin complex is relatively constant in normal rabbit and dog blood. It is not reduced by dicumarol even after the prothrombin activity falls to a very low level.

[10] Quick, A. J., and Stefanini, M., *J. Lab. Clin. Med.*, 1949, **34**, 973.

[11] Quick, A. J., and Stefanini, M., *J. Lab. Clin. Med.*, 1949, **34**, 1203.

[12] Owen, C. A., and Bollman, J. L., PROC. SOC. EXP. BIOL. AND MED., 1948, **67**, 231.

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Intracellular Bile Canaliculi in the Rabbit Liver. (17391)

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There is no controversy as to the general pattern of the bile canaliculi in the mammalian liver with but one exception. This concerns the existence of intracellular branches.

Gomori's[1] technic for the histochemical demonstration of alkaline phosphatase furnishes a very convenient method for the study of the bile capillaries under normal and abnormal conditions, since the bile canaliculi in the liver of some species show striking staining properties.[2-4] The results obtained with this method in the liver of rabbits under normal conditions and after experimental biliary obstruction, strongly suggest the existence of intracellular branches.

Material and Method. In medium sized rabbit under ether anesthesia, a liver biopsy was taken and the cystic and bile ducts were ligated. Twenty-two animals were allowed to survive from 1 to 31 days. In addition, livers from normal animals were available. Sections from tissues fixed in cold acetone were stained with Gomori's method[1] as modified by Kabat

[1] Gomori, G., PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 23.

[2] Gomori, G., *J. Cell. and Comp. Physiol.*, 1941, **17**, 71.

[3] Wachstein, M., and Zak, F. G., PROC. SOC. EXP. BIOL. AND MED., 1946, **62**, 73.

[4] Jacoby, F., *J. Phys.*, 1947, **106**, 23P.

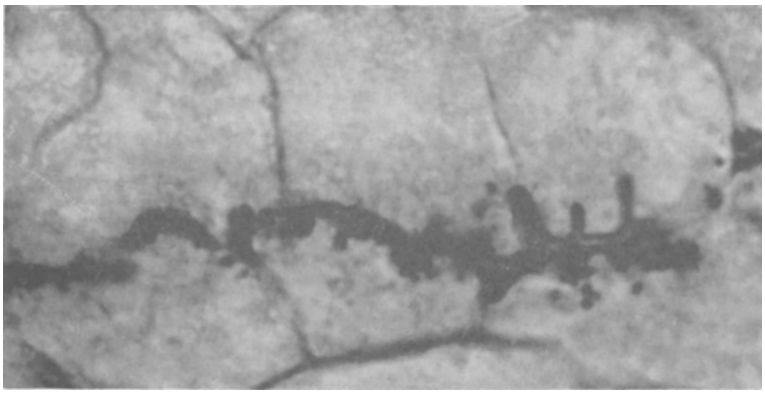

FIG. 1.
Gomori's stain for alkaline phosphatase. Prominent staining of bile capillaries in the normal rabbit liver. Accumulation of granular phosphatase around bile canaliculi. Note intracellular branches. × 1400.

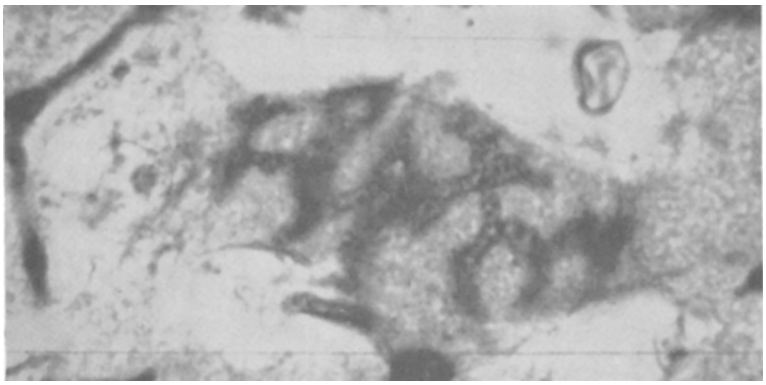

FIG. 2.
Dilatation of bile capillaries 4 days after biliary obstruction. Note intra cellular network. × 1400.

and Furth.[5] Sections were incubated for 2 hours.

Results. The distribution of alkaline phosphatase activity in the normal liver of the rabbit was quite similar to that previously described in the dog liver.[3] Surrounding the distinctly outlined bile capillaries, granular deposits of alkaline phosphatase were often seen.[6] Fig. 1 shows an intercellularly located bile capillary situated between 2 liver cell cords. From this axial canaliculus, not only intercellular blind ending branches, but also short intracellular ramifications are seen to spring off. These intracellular branches often stain as black lines but occasionally show a distinct lumen. By using the fine adjustment screw under oil immersion, one can be reasonably sure that the short branches lie really within the cell and do not represent portions of communicating intercellular ramifications. Although very short, nob like outpouchings are quite common, larger intracellular branches, as pictured in Fig. 1 are not too frequent in the normal liver. In livers of rabbits which survived the experimental biliary obstruction from 4 to 31 days, however, there occurred not only marked dilation and tortuosity of bile capillaries but intracellular

[5] Kabat, E. A., and Furth, J., *Am. J. Path.*, 1941, **17**, 303.

[6] Deane, H. W., and Dempsey, E. W., *Anat. Rec.*, 1945, **93**, 401.

branches also became quite numerous. Fig. 2 depicts a network of bile canaliculi located within 2 liver cells. The intracellular branches are seen to possess a real lumen.

Discussion. In most modern textbooks of histology, no mention is made of intracellular bile capillaries. Their possible occurrence is conceded in Sharpey-Schafer's[7] and Stöhr's textbooks.[8] Their existence, however, is denied by Maximow and Bloom.[9] The study of finer morphological details with the phosphatase staining technic is considerably helped by the fact that in contrast to the dog liver, the rabbit liver, after biliary obstruction shows no appreciable increase of cytoplasmic phosphatase activity such as often blurs the outline of the dilated capillaries. Clara,[10] using special staining technics, considers the occurrence of intracellular branches in the rabbit liver as likely, but not as definitely, proved. He pointed out that an intracellular location may seemingly be present, while in reality it is due to a location of bile capillaries on the surface of the liver cells in question. While the possibility of this cannot be completely excluded, in the case of the normal rabbit liver, it is quite unlikely in that of the liver after biliary obstruction. Here, a network of dilated bile capillaries is frequently observed on the same plane within a single liver cell. Occasionally, it is found at the level of the cell nucleus.

Summary. With the aid of the histochemical phosphatase stain, intracellular bile canaliculi can be demonstrated in the normal rabbit liver. These intracellular branches become considerably more pronounced following experimental biliary obstruction.

[7] Sharpey-Schafer, E., Essentials of Histology, Descriptive and Practical for use of students. 13th edition by M. Carleton, London, New York, Toronto.

[8] Stohr, P., Lehrbuch der Histologie und der Mikroskopischen Anatomie des Menschen., 25th edition by W. V. Mollendorf, Jena 1943, p. 349.

[9] Maximow, A. A., and Bloom, W., Textbook of Histology, Philadelphia and London, 1947, p. 43.

[10] Clara, M., *Z. F. Mikr. Anat. Forsch,* 1934, **352**, 1.

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Enzymatic Hydrolysis of Benzoylarginineamide by Normal and Tuberculous Tissue of Rabbits.* (17392)

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Caseation has been described by Rich[1] in these words, "When, as a result of partial autolysis, necrotic cells lose their structure and outlines, and their remains together with intercellular materials tend to become fused into a formless, coagulated and more or less inspissated mass, the process is termed caseation." In rabbits, experimentally infected with virulent tubercle bacilli, caseation is usually observed about the third week of the disease, when according to Lurie,[2] the monocytes, which make up the bulk of the cellular material in the caseous area, have been transformed into epithelioid cells and allergy to tuberculin has developed. This suggests that the process of caseation is associated with some degree of acquired tissue immunity or resistance to infection with tubercle bacilli.

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[1] Rich, A. R., The Pathogenesis of Tuberculosis, C. C. Thomas, Publ., Springfield, Ill., 1946, p. 733 ff.

[2] Lurie, M. B., *J. Exp. Med.*, 1933, **57**, 181.