and to the promotion of public health. Park's great achievement was the establishment of the highly efficient public health service for the world's greatest city. The details of his career show why he was cited as "the perfect type of a scientist in the service of the state."

Among the many brilliant leaders who made the Johns Hopkins Medical School so great is Lewellys F. Barker, a Canadian Quaker, who studied in Toronto and Europe, served in the Philippines and in India, and succeeded Osler as head of the Department of Medicine at Hopkins. Later he gave up his full-time university work to engage more in practice and public work of a broad social nature.

The development of pediatrics has been one of the outstanding achievements of modern medicine. An American pioneer and influential leader in this was Luther Emmett Holt (1855–1924). Most of Holt's career was spent in New York City, although he traveled extensively and participated in professional work in Europe and China, after World War I. Like most leaders in American medicine, Holt was a prodigious writer, and his texts relating to his specialty have been standard in medical literature for years.

Hugh Hampton Young's autobiography is vigorous and entertaining. It paints an astonishing picture of contrast between serious citizenry, merry-making buffoonery and careful meticulous technique in surgery. The volume is unusual in containing a considerable amount of technical material relating particularly to the study of urology, which Dr. Young has been so instrumental in promoting. There are intriguing chapters on World War I medicine, Diamond Jim Brady, excursions of all sorts to all parts of the world, and a remarkable series of pen pictures of his many brilliant associates at Hopkins. It also contains the story of mercurochrome, but not quite complete.

Hans Zinsser's remarkable autobiography is a brave and brilliant apology for modern culture. His religious and romantic impressions are sensitive poetry; his anecdotes are delightful; his descriptions of his professional work, particularly in Serbia, Russia, Tunis and the Orient, emphasize the political difficulties of applying modern knowledge to human welfare, and through it all his philosophical confusion resolves into a long-range optimism which even impending death can not dispel.

Significant as a group is this baker's dozen of recent biographies and autobiographies relating to medical leaders. They indicate the dependence of American medical science on its European sources—a dependence melting now into a common pool of scientific achievement with our English colleagues. Whereas American medicine stems from sturdy Scotch and English roots, it has been abundantly grafted with French and German buddings. Many of these are now being trimmed away. It remains to be seen whether the stock will be able to carry the heavy potentialities of Russian or Chinese or Latin-American medical ideas which are certain to flourish among us if given a chance.

CHAUNCEY D. LEAKE

MEDICAL SCHOOL,
UNIVERSITY OF TEXAS,
GALVESTON

SPECIAL ARTICLES

HEPARIN AND THE ANTITHROMBIC ACTIVITY OF PLASMA[1]

THE antithrombin of plasma destroys thrombin almost as rapidly as the latter is formed. Eventually, the serum, expressed from the clot, is found to contain merely traces of prothrombin and thrombin.

On adding heparin to plasma, the antithrombic activity is known to be "increased." We shall show, however, that heparin does not increase the total capacity of plasma to destroy thrombin; it merely increases the speed with which it does so. The heparin thus appears to behave merely as a catalyst in the destruction of thrombin.

Fig. 1 illustrates the relationships which were found. Into each of 4 tubes were placed 3,880 units of purified thrombin. To one (A) was added heparin alone, to another (B) was added plasma, to a third (C) and a fourth (D) were added both heparin and plasma. All tubes were made up to constant volume and were then allowed to stand for an hour. During that time the thrombin concentration was repeatedly measured. The heparin alone (Curve A) had no effect. The most striking change was shown by the tube (D), containing plasma, together with 0.5 Toronto units of heparin. Here the thrombin titer fell precipitously to the 1,500-unit level within a minute. It then remained at that level throughout the course of the experiment. With only 0.1 unit of heparin (curve C) the thrombin titer also fell to the 1,500-unit level, but 15 minutes were required instead of one.

From these experiments it is evident that the amount of co-factor determines the amount of thrombin destroyed; the amount of heparin determines the *speed* of destruction.

[1] This work was aided by a grant from the John and Mary R. Markle Foundation. Funds for a technical assistant were also supplied by the Graduate College, State University of Iowa.

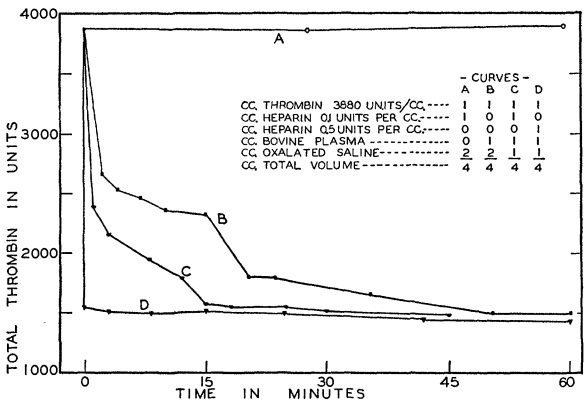

FIG. 1. The thrombin and the heparin were dissolved in oxalated saline (0.075 per cent. $K_2C_2O_4$ + 0.80 per cent. NaCl). Oxalated bovine plasma was obtained from a mixture of 7 parts blood and 1 part 1.85 per cent. $K_2C_2O_4$. The thrombin unit is the amount required to clot 1 cc of purified fibrinogen solution, containing calcium and acacia, in 15 seconds. In these experiments, calcium was omitted in order to avoid forming thrombin from the prothrombin present in the oxalated plasma. Under these conditions (*Am. Jour. Physiol.*—in press), thrombin is one third less efficient; the thrombin titers were therefore multiplied by the factor, 1.5, and the results were then plotted in terms of standard units.

In light of these findings, it is of great interest that plasma alone, without a supplement of heparin, also caused the thrombin titer to fall to the 1,500-unit level (tube B). The fall occurred quite slowly, however—almost an hour was required. It is known that plasma contains small amounts of heparin, and this heparin may be an essential catalyst, without which the reaction can not occur in finite time. It will be necessary to isolate the co-factor in order to determine whether, in the absence of heparin, it possesses any detectable antithrombic activity. It may well be that it does not.

WALTER H. SEEGERS
E. D. WARNER
K. M. BRINKHOUS
H. P. SMITH

STATE UNIVERSITY OF IOWA
IOWA CITY

THE ULTRAVIOLET SPECTROGRAPHIC EXAMINATION OF THE FAT FRACTION OF MOUSE MILK AND MAMMARY GLANDS[1]

THE presence of a mammary tumor-producing substance in the milk of high tumor strain mice has been adequately demonstrated by Bittner,[2] Andervont,[3] DeOme.[4] It is known to be present also in the blood and certain tissues of high tumor strain females.[5,6] If this factor is similar to the estrogens or known synthetic carcinogenic hydrocarbons, it should be demonstrable by a comparison of the ultraviolet absorption spectra of the fat fractions of the milk and the mammary glands of high and low tumor strain mice. Milk and non-tumorous mammary glands from lactating high tumor strains, A, C3H and dba and from the low tumor strain C57Black were studied.

Milk was obtained by means of a miniature milking machine. Only mammary glands engorged with milk were used. Freshly excised mammary glands were plunged into liquid air and macerated with CO_2 as described by Strait and Aird.[7] The macerate was extracted by a solvent-separation procedure involving the use of acetone, ether, alcohol and isooctane. Alcohol soluble and insoluble fractions were studied independently. Preliminary control experiments indicated that extreme care is necessary in the use and purification of solvents if spurious results are to be avoided. The extraction procedure permitted study of the ultraviolet region down to 2300 Å, a range sufficient to include compounds of the type expected. Five samples of milk from A and C57Black mice averaging 3.26 g and eleven samples of mammary glands averaging 3.62 g were used. The absorption spectra of the extracts in spectroscopically pure isooctane were photographed in the ultraviolet with a Hilger medium quartz spectrograph. The extraction procedure is known to recover 1, 2, 5, 6-dibenzanthracene and the estrogens triphenylethylene and oestradiol.

A comparison of the ultraviolet absorption spectra of milk and mammary glands of high and low tumor strain mice showed no significant differences. These results would indicate that (1) the milk-borne factor either is not carried in the fat fraction or, if it is (2) it is not spectrographically similar to the carcinogenic hydrocarbons or estrogens, or (3) it is present in quantities too small to be detected spectrographically. Triphenylethylene may be detected in concentrations of 0.025 milligrams per gram, the naturally occurring estrogens in somewhat higher concentrations, and the carcinogenic hydrocarbons in lower concentrations.

Since the initiation of these experiments, recently published ultracentrifugation data[8] have indicated also that the active agent is primarily in the non-fat fraction. Ultrafiltration experiments by one of us on

[1] This work was in part supported by a grant in aid from the Blanche and Frank Wolf Foundation. The authors wish to express their appreciation to Dr. I. H. Perry for her valuable counsel.

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