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Gersh I & Catchpole H R. The organization of ground substance and basement membrane and its significance in tissue injury, disease and growth. *Amer. J. Anat.* 85:457-521, 1949.
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The significance of this work was related to the use of freezing-drying and the use of a specific histochemical agent. Together, these enabled us to formulate a concept of "organization" of basement membrane and ground substance matrices existing in different states of solubility or polymerization depending upon physiological and pathological tissue state, inflammation, and tumor growth and spread mediated by tissue collagenases. Also studied was the relation between serum and tissue glycoproteins. [The *SCI*® indicates that this paper has been cited in over 420 publications since 1955.]

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This work grew out of a post-World War II experiment in which the late Granville A. Bennett, who became head of pathology at the University of Illinois College of Medicine in 1945, appointed basic-science PhDs as full members of the department—and then left them alone. Isidore Gersh and I—an officer and a sailor—had come together as improbable members of a scientific team while working on problems of bends and aeroembolism at the Naval Medical Research Institute in Bethesda, Maryland, at its inception in 1942-1943. Gersh was a brilliant anatomist, and by the technique of freezing and drying, which he pioneered, we were able to trap and detect gas bubbles in blood and tissues.[1] Incidentally, his first scientific instruction to me (known in the Navy as an order) was to "learn Italian"; it was a logical one since the human pathology literature largely concerned the sponge divers of the Adriatic Sea.

In 1946, after three and a half years of variously sidetracked "careers," we set up our laboratory in Chicago and struck out in various directions, sometimes, but not always, related to previous interests dating to the early 1930s. Thus we ventured into growing hepatomas and cancers in rats and into cell fractionation of tumors after the techniques of Gersh's teacher, Robert R. Bensley, then still hale and active at the University of Chicago. Gersh pursued an old interest in the Golgi apparatus. I fractionated sheep anterior pituitaries by particle size and distribution and tested some fractions for hormonal activity. This soon became ruinously expensive, so I shifted to histochemistry, of which Gersh was, of course, already a master.[2] Gersh set up an ultraviolet microscope dominated by a hand-built, water-cooled mercury lamp with a half-life of about two minutes, which generated instant floods and crises in our makeshift darkroom. But our first postwar overseas visitors, John Bradfield and Maurice Errera, worked with it successfully. We bought a high-speed centrifuge attachment and enclosed our cast-iron centrifuge shell with a quarter-inch shield of armor plate kindly donated by an old Navy friend, Jackson Spear, who trembled for our safety.

Graduate students appeared. Connective tissue had been an old love of Gersh's through the influence of Sylvia Bensley's remarkable studies in the 1930s. Now, with the work of Karl Meyer and F. Duran-Reynals, it was "back" as a legitimate object of study. When the periodic acid-Schiff reagent was introduced[3,4] and given chemical significance by R.D. Hotchkiss,[5] we launched many experiments culminating in the *Classic* paper. Gersh always attempted to apply histochemistry to the solution of real problems rather than to random "staining."

In 1949 concepts of greater or less polymerization or aggregation thus applied were unwelcome to biochemists and others and gave us plenty of trouble. However, the ideas were promptly applied by other friends and associates: by Robert Lewert to the penetration of skin by cercariae; by Milton Engel to the calcification and resorption of bone and cartilage and to periodontal disease; by Eve Perl to the effects of relaxin; and by medical student Tom Harter, who discovered the glycoprotein nature of the zona pellucida.

Other results were the reports by Gersh on the glycoprotein nature of thyroglobulin[6] and the contents of the Golgi,[7] and the article by me on the localization of gonadotrophic hormone in pituitary basophils. This work was updated in 1960[8] to introduce the concept of a two-phase system for connective tissue matrices. A final review in 1982[9] is dedicated to the memory of Gersh.

Following this report our academic paths separated but our interests remained close. Gersh in Philadelphia applied his cryobiology and cryochemistry techniques to ultrastructure. The Illinois group including Engel, N. Joseph, and me developed a thermodynamic theory of ions in connective tissue and cells.

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2. **Gersh I.** Recent developments in histochemistry. *Physiol. Rev.* 21:242-66, 1941.
3. **McManus J F A.** Histological demonstration of mucin after periodic acid. *Nature* 158:202, 1946. (Cited 820 times since 1955.)
4. **Lillie R D.** *Histopathologic technic.* Philadelphia: Blakiston, 1948. 300 p. (Cited 225 times since 1955.)
5. **Hotchkiss R D.** A microchemical reaction resulting in the staining of polysaccharide structures in fixed tissue preparations. *Arch. Biochem.* 16:131-41, 1948. (Cited 865 times since 1955.)
6. **Gersh I.** Glycoproteins in the thyroid gland of rats. *J. Endocrinology* 6:282-7, 1949-50.
7. ————. A protein component of the Golgi apparatus. *Arch. Pathol.* 47:99-109, 1949.
8. **Gersh I & Catchpole H R.** The nature of ground substance and connective tissue. *Perspect. Biol. Med.* 3:282-319, 1960. (Cited 160 times.)
9. **Catchpole H R.** Connective tissue, basement membrane, extracellular matrix. (Ioachim H L. ed.) *Pathobiology annual 1982.* New York: Raven Press, 1982. Vol. 12. p. 1-33.

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