I.1 GENERAL INTRODUCTION AND A BRIEF HISTORY OF AMYLOIDOSIS

and Background of the Groningen, Helsinki, Oporto and Harriman Amyloid Symposia

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1. Amyloid: a historical perspective

Literary research into the history of amyloid is fascinating, and underscores the complexity of scientific discoveries, the blending of different ideas and concepts, the overlap of new and old information and the ultimate evolution of scientific truths. It also underscores the importance of nomenclature as a unifying force in delineating to scientists whether or not they are talking about the same disease, the same syndrome, the same phenomenon. This is particularly important in dealing with ill-defined entities.

Just as there are milestones and key treatises in the elucidation of scientific events, there are milestone reviews, which in the past quarter century have inabled us to trace with reasonable accuracy, the early history of amyloidosis. The treatise of Schwartz (1970) (1) and the papers of Puchtler and Sweat (1966) (2), of Letterer (1968) (3), of Aterman (1976) (4,5) and several other papers (6-8) are major guideposts to the study of early data.

Since there was no terminology by which amyloid was uniquely described until its name was popularized by Virchow in 1854 (9-12), it is difficult to be sure of its true origins. Was the lardaceous liver or the waxy liver always amyloid? Was the spongy and "white stone" containing spleen always an amyloid spleen? While we shall never know precisely, clearly entities consistent with amyloid were described in autopsies carried out as early as 1639 (by Nicolous Fontanus), in 1657 (by Thomas Bartholin), in works by Theophile B. Bonet (1620-1689), Malpighi (1628-1694), Morgagni (1682-1770) and others (1). Portal in 1813 was felt by Dr. Schwartz to be the first to compare what was probably amyloid to "lard" and to "tallow". Rokitansky in 1842 (13) described the "waxy" liver variety of the lardaceous liver and splenomegaly consistent with amyloid, as did Budd in 1845 (14). An Edinburgh group (15) apparently without knowledge of Virchow's work described cases in which liver, spleen and kidney were affected with waxy substances, certainly
consistent with amyloid.

Rokitansky and Budd are often given credit for the first descriptions of amyloid although clearly the earlier pathologists had encountered this substance. The key to progress, however, lay in Virchow's assigning to this substance a name, and the fascinating prevailing philosophy and medical knowledge of that era. The name ultimately has its root in the Latin-Amylum and Greek-Amylon. When Virchow discovered that the corpora amylacea stained pale blue on treatment with iodine, and violet on the addition of sulfuric acid, he had no doubt that these bodies were composed of cellulose and at age 32 sent his report to the French Academy (1). His successor as prosector at a Berlin hospital, H. Meckel (1821-1856), however, was considered by Schwartz as "truly the author who inaugurated the exploration of the disease we presently call amyloidosis" (Schwartz, p. 296). Meckel's interest was in the application of the iodine-sulfuric acid test to other organs, and he was able to demonstrate the "lardaceous" material in liver, spleen, kidney, aorta, arteries and intestinal wall. He preferred the name cholesterin and a lively debate with Virchow ensued (16). Virchow himself disagreed with Rokitansky in that the latter's "waxy" liver appeared "lardaceous" to him. He seemed to believe that there was a difference between the two, and that the waxy spleen derived from the degeneration of tissue compounds. The universal use of the term amyloid for tissues or organs staining positively with iodine-sulfuric acid was, however, established and the debate about the similarity or lack of similarity of cerebral corpora amylacea to the tissue lesions and Virchow's views as to the nature of amyloid degeneration were less in vogue.

Aterman (4,5) has nicely reviewed the historical, translational and indeed modern confusion that arose in the seventies based on the usage of the term amyloid, its derivation, original use and historical meaning. Clearly, as noted above, what we now accept as amyloid was known to pathologists as "waxy" or "lardaceous" abnormalities for centuries before Virchow; what we accept as having been coined by Virchow, (i.e. the term amyloid) was used by Schleiden (17) and by Harting (18) before him. Indeed, the modern confusion over Virchow's use of the term amyloid (i.e. starch vs. cellulose) has been clearly shown by Puchtler and Sweat (2) as having been used to indicate cellulose in paper after paper. Interestingly, the improper attribution, i.e., that Virchow regarded amyloid as starch rather than cellulose, took place as early as 1854 through the work and translations of Busk (19). The argument of starch vs. cellulose was far more poignant in the 1850's than it is today, for then scientific debates about the separation of the plant and animal kingdoms were prominent, -and to find so called "cellulose" in the brain of the human body was truly remarkable. Indeed Harting (18,4), who helped develop the iodine-sulfuric acid method in 1847 (and whom Virchow quoted) used the term amyloid as meaning cellulose.

Thus, the major method of diagnosing amyloid was the use of the iodine-sulfuric acid stain, when in 1875 Cornil (20), Heschl (21) and Jurgens (22,5) independently discovered that amyloid deposits stained