References


An Invitation For A Genetic Study
Milroy's Disease (Hereditary Lymphedema)

... In 1928 Milroy published a follow-up on the family with lymphedema ..., which was first reported in 1892. The propositus was at that time still alive in his late 60's and was active as a missionary in Burma. Affected members of the family also included a clergyman in Florida (who had died before 1928), a congressman, a U. S. senator, and a Chicago physician (also deceased), who had served as a surgeon in the U. S. Navy in the Civil War.

Surely affected members of that family are still living. The account of the fortunes of the family with regard to the ailment might profitably be updated, now 40 years after Milroy's follow-up. My colleagues and I have found this sort of long-term, indeed multi-generation follow-up useful from the standpoint of both the genetics of the entity and its natural history. ... I would urge that some physician, caring for present day bearers of the "original" Milroy, gene chart the odyssey of the gene during the last 40 years.—Victor A. McKusick: Letters to the Editor. JAMA 204: 832, 1968.
Venous Return vs. Venous Pressure

Effect of alteration in venous supply on volume of heart. Read from left to right.

Dog 5: 15 kg; heart 67 grms.

<table>
<thead>
<tr>
<th>A.R.</th>
<th>R.P.</th>
<th>V.P.</th>
<th>Rate</th>
<th>O.P. per beat</th>
<th>O.P. per beat observed</th>
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Mitral Stenosis and Angina Pectoris
John Hunter (circa 1790)

Rheumatic Heart Disease

John Hunter before his death in 1793 had collected a whole set of specimens of rheumatic carditis. The condition was first recognized in print in 1797. Perhaps the most impressive of these is . . . [depicted in] Fig. 1b, which shows severe mitral stenosis with a very large left atrium. Of this Hunter writes, “The diminished size of the aperture between the auricle and the ventricle deserves particular notice.” This specimen very probably belongs to a Miss Wood whose case history Hunter gives in detail (Hunter, Ms. c). For two years she suffered from dyspnoea and substernal pain. At autopsy, Hunter found the signs of congestive heart failure. “In the heart itself,” he writes, “the left auricle was thicker in its coats than common, particularly near the ventricle. The valvulae mitrales adhered to one another all round; were become extremely thick and hard, by which means they must have lost a considerable deal of their intended use; the blood must have found a passage back to the auricle.” Aortic valvular disease was also present with thickened valve cusps. Hunter tells how Dr. Heberden had been consulted, and had accepted the patient’s substernal pain as a true example of angina pectoris. This must surely be the earliest instance of the recognition of angina pectoris as a symptom of mitral stenosis. Unfortunately the case is undated.—KENNETH D. KEELE: John Hunter’s Contribution to Cardio-vascular Pathology. Ann Roy Coll Surg Eng 39: 248, 1966.
Century of Asthma Deaths
A Recent Increase?

Should finger be pointed at isoproterenol?


300 Years Ago

Paradoxical Pulse

The wife of a certain citizen of London, aged 30, healthy and active enough previously, became very dejected and melancholy during the last three years of her life, suffered from breathlessness on the least exertion, had a small and often an intermittent pulse, and complained almost continuously of attacks of pain and of great physical discomfort [p. 100] in the precordium. . . . we discovered a pathological condition of the heart, to which we may rightly attribute the cause of all her troubles. The thorax was opened and the lungs were healthy enough; the pericardium, however, had become closely attached all over to the whole surface of the heart, so that it could only with difficulty be separated from it. Further, this membrane had become thick, opaque, and hard, instead of being thin and transparent, as it should naturally have been. Hence, as there was no space for the free movement of the heart, and no fluid for moistening its surface, it is little wonder that she complained all the time of these ills. Further, as the diaphragm is always attached to the pericardium in man, when the heart itself was also united to [p. 101] the pericardium, the diaphragm must of necessity have carried the heart down with it at every inspiration, and during that time must have held up and suppressed its movement. So the observed intermission of the pulse succeeded regularly at every inspiration.—Richard Lower: Tractatus de Corde item de Motu & Colore Sanguinis et Chylis in eum Transitu. (1669) Translated by K. J. Franklin. In: R. T. Gunther: Early Science in Oxford, vol. 9, Oxford, University Press, 1932, ch. 2.
in previous studies employing methyldopa, guanethidine, or pargyline in combination with diuretic agents\textsuperscript{5,8,9} (table 7).

References

à la Proust

Man responds not as a mechanical assemblage of parts, but as an integrated organism with a complex history. Any physicochemical or psychic stimulus which impinges on him sets in motion a host of secondary processes with very indirect and often delayed effects. Seeing an object which recalls an article of food may stimulate appetite or cause nausea; smelling an artificial perfume may evoke the heat of a summer day, or the chill of a fall evening; hearing a faint but unexpected noise at night may cause either a rise or fall in blood pressure. In other words, the ultimate physiological or mental expression of stimuli commonly has little bearing on their primary direct effects.—RENE DUBOS: Hippocrates in Modern Dress. Proc Inst Med Chicago 25: 247, 1964-65.


A New Ecclesiastes

Human life being so profoundly influenced by the evolutionary, experimental, and social past, it is certain that the science of man cannot possibly be based exclusively on knowledge of the reactions exhibited by components isolated from the body. The past, like the mind, disappears when the organism is taken apart. The statement that most responses involve the whole organism functioning as an integrated unit is so obvious as to seem trivial. But it has large implications for medical teaching and medical research.

The time has come to give to the study of the responses that the living organism makes to its total environment the same dignity and support which is being given at present to the science of parts and reactions isolated from the organism. Exclusive emphasis on the reductionist approach will otherwise lead medicine into blind alleys. Unless a program of organismic and environmental research is vigorously prosecuted, medicine will be unable to support the loads placed on it by the health problems arising from the new environmental forces created by modern life.—René Dubos: Hippocrates in Modern Dress. Proc Inst Med Chicago 25: 249, 1964-65.
Pulmonary Valve Incompetence
(Graham Steell Murmur)

. . . I wish to plead for the admission among the recognized auscultatory signs of disease of a murmur due to pulmonary regurgitation, such regurgitation occurring independently of disease or deformity of the valves, and as the result of long-continued excess of blood pressure in the pulmonary artery.

I am prepared for the objection that the murmur under consideration is only the murmur of a slight amount of aortic regurgitation, the usual evidence of which in the pulse is masked by the mitral lesion.

The murmur of high-pressure in the pulmonary artery is not peculiar to mitral stenosis, although it is most commonly met with, as a consequence of this lesion. Any long-continued obstruction in the pulmonary circulation may produce it. The pulmonary valves, like the aortic, do not readily become incompetent, apart from structural change. Probably no amount of blood pressure in the pulmonary artery will render them so suddenly, as, at least, theoretically, the mitral valves may be rendered incompetent. Changes in the vessel, with widening of its channel, and, eventually, of its orifice, long precede the occurrence of incompetence of its valves.

. . . To those to whom neither the dogmatic assertion that all such murmurs as I have described, are, in spite of the absence of any confirmatory evidence, aortic in origin, nor the sceptical non possumus of Doctor Fagge, commends itself, I would urge a careful consideration of "the high-pressure murmur of the pulmonary artery" as a feasible explanation. I have stated my own opinion; from others I ask only that this murmur should find a place—however subordinate—among the physical signs of disease which they recognise.—GRAHAM STEELL: The Murmur of High-Pressure in the Pulmonary Artery. In WILLIUS, F. A., AND KEYS, T. E.: Classics of Cardiology, vol. 2. New York, Dover Publications, Inc., 1941, p. 681.