Commentary

Atherosclerosis in Young People

The Value of the Autopsy for Studies of the Epidemiology and Pathobiology of Disease

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In this issue of *The American Journal of Pathology* we publish a summary of the major results of a research project initiated in 1985. Titled "The pathobiological determinants of atherosclerosis in youth" (PDAY), the study was directed by Drs. R. W. Wissler of the University of Chicago and J. P. Strong of Louisiana State University and involved 14 centers. Investigators examined material obtained from forensic autopsies of more than 3000 individuals between the ages of 15 and 34. These individuals had no evidence of cardiovascular or other chronic disease; most died as a result of trauma. Although more than 75 papers based on this material have already been published, I feel that it is useful to compile a summary of these observations. In their paper, Wissler et al¹ outline the protocols developed for the project, highlight its more significant results, and present some important guidelines for the prevention of cardiovascular disease in young people. I also want to emphasize the essential role that forensic autopsies played in these studies.

There has been much debate about the role of the autopsy in present-day medical practice, teaching, and research. Rosai has argued that to be a tool of real value rather than an exercise in tradition, autopsies need to be done selectively and efficiently, yielding final diagnoses rapidly so that findings can be integrated meaningfully with clinical data, as is the case for surgical specimens.² Asking specific questions before an autopsy is performed permits the collection of material that can best answer these questions and can be used for further studies involving biochemical and molecular techniques. These were the goals of the PDAY research program protocols. The project has been very successful in reaching these goals using tissues obtained at autopsy as the basis for correlations of morphological, biochemical, and epidemiological data. The next phase of the project will, I hope, extend these studies to the analysis of molecular

markers of atherosclerosis derived from recent studies in humans and animal models. The new studies should aim to establish precise pathogenetic mechanisms that determine the progression of atherosclerosis in young people.

As stated by Wissler et al, "the results of the (PDAY) study reflect the state of atherosclerosis development in young people living in the U.S.A. late in the 20th century." Among the many important findings reported, I call your attention to these:

1. All U.S. teenagers sampled had fatty streaks in some segment of their arterial system.
2. Intermediate lesions (fatty plaques) developed from fatty streaks in the aorta and coronary with wide age variation but the extent of the lesions increased steadily from 15 to 34 years, as measured in 5-year age-group intervals.
3. Raised lesions were detected earlier in the aorta than in coronary arteries; lesions containing lipids were present in the aorta of 15- to 20-year-old individuals.
4. The presence of coronary artery lesions having concentric microarchitecture and a large number of inflammatory cells was correlated with the presence of circulating immune complexes.
5. Obesity was a positive risk factor for the development of vascular lesions.
6. Raised lesions in the abdominal aorta were greatly increased in smokers in the 25–34 age group.
7. Smoking and hypertension had the greatest effect on the development of advanced plaques in young adults (approximately 6-fold and 4-fold increased incidence, respectively).
8. Ten percent of the individuals in this study had advanced atherosclerosis consisting of plaques with necrotic fat-filled centers and fibrous caps. Approximately 80% of these individuals were smokers.

It is debatable whether the presence of fatty streaks in individuals 15 to 34 years of age has pathogenetic importance for the development of atherosclerosis.

However, it is truly alarming that 10% of individuals in this age group had advanced atherosclerosis. There is no reason to believe there was a bias in the selection of cases for study. Indeed, I agree with Wissler et al that the PDAY cases represent a random sample of U.S. youth. Do all individuals with advanced lesions have gene mutations known to predispose one to atherosclerosis? Answers to this question and many others remain to be determined. The material used in the PDAY project is available to the scientific community through the administrative center at Louisiana State

University. I hope that publication of the paper by Wissler et al will further increase the use of this material for scientific investigation of the causes and progression of atherosclerosis.

References

1. Wissler RW, Strong JP, PDAY Research Group: Risk factors and progression of atherosclerosis in youth. *Am J Pathol* 1998, 153:1023–1033
2. Rosai J: The posthumous analysis (PHA): an alternative to the conventional autopsy. *Am J Clin Pathol* 1996, 106:S15–S17