Acute myocardial infarction is one of the most common causes of death in the United States and every conceivable approach (experimental, clinical, anatomical and epidemiological) is being utilized in an effort to dispel the mystery that surrounds it. As part of the wide approach to the study of the disease, Drs. Wilbur A. Thomas, Kyu Taik Lee, Robert M. O’Neal and Erwin R. Rabin, pathologists at Washington University in St. Louis, have recently determined the incidence of acute myocardial infarction in several large series of autopsies that were performed between 1910 and 1954. Some of the results of their studies have been reported (Arch. Int. Med. 97, 421 (1956); Ibid. 98, 80 (1956); Ibid. 98, 489 (1956); Arch. Path. 60, 616 (1955); Am. Heart J. 52, 581 (1956)) and other results will be reported in subsequent articles.

Every autopsy from Barnes Hospital was classified by age, sex, race and period of death (1910 to 1930 or 1940 to 1954) and the incidence of acute myocardial infarction was determined for each decade of life, each sex, each race and each period. The data obtained were correlated with information regarding the incidence of diabetes mellitus, obesity and hypertension in the various groups. Similar, though more limited, studies were made of the autopsy series at Homer G. Phillips Hospital in St. Louis, Charity Hospital in New Orleans, and Howard University Hospital in Washington. An acute myocardial infarct as defined in these studies indicates histologically recognizable death of cardiac muscle of less than one month’s duration. The duration was determined as accurately as possible by the clinical history and anatomical findings. In most instances the myocardial infarct was due to occlusion of an atherosclerotic coronary artery by a thrombus.

Investigators in the past have almost invariably found a higher overall incidence of myocardial infarction among White men than among White women (see P. D. White, Heart Disease, Macmillan, New York (1951)). In studies based on clinical diagnoses the relative incidence in the two sexes have varied from 3:1 to 7:1 (males:females). Very little information is available from autopsy series because most investigators reporting data from the latter source have simply stated the number of patients of each sex with coronary arteriosclerosis and its complications and have not determined the ratio of the sexes in the entire autopsy population. It obviously is necessary to know the sex distribution in the population being analyzed before one can determine the relative incidence of a disease in the two sexes. One cannot assume that the sexes will be evenly divided in a large autopsy series. Most series that have been analyzed, including the series at Barnes Hospital, contain considerably more men than women. However, data regarding the relative incidence of myocardial infarction are available from at least one other large autopsy series covering the period 1910 to 1938. Among 30,265 autopsies performed at the University of Minnesota during the period of 1910 to 1938, Clawson (Am. Heart J. 22, 607 (1941)) found the ratio of the incidence of deaths from coronary arteriosclerosis to be 2.5 males to 1 female.

The most remarkable data obtained from the Barnes autopsy series are those pertaining to changes in the relative sex incidence of acute myocardial infarction. In the period 1910 to 1940, the incidence of acute myocardial infarction in the Barnes autopsy series was 2 males to 1 female. This difference in incidence in the two sexes is much less than that in most studies based on clinical diagnoses but is quite similar to the ratio of...
2.5 to 1 reported by Clawson in the Minnesota autopsy series for the years 1910 to 1938. Thus, prior to 1940, data from several different sources indicated that the overall incidence of coronary arteriosclerosis and its complications was greater in men than in women. When the period 1940 to 1954 was studied by the group at Washington University it became apparent that a startling change had occurred. In the Barnes autopsy series for the period 1940 to 1954, the ratio of the incidence of acute myocardial infarction in the two sexes approaches 1:1 (actually 1.1 male to 1 female, which is not a significant difference in this series). After the completion of the study of the Barnes autopsy series, similar data were obtained regarding recent periods from two other autopsy series. Achor, Burchell and Edwards (unpublished data quoted by Lee and Thomas in Arch. Int. Med. 98, 80 (1956)) found a similar ratio of incidence of acute myocardial infarction (1:1) between the sexes among patients autopsied at the Mayo Clinic during the period 1946 to 1950. The group at Washington University was allowed to examine a large sample of the autopsy series at Charity Hospital in New Orleans and they found in the period 1940 to 1954 that the incidence of acute myocardial infarction was actually higher in White women than in White men. (However, the difference was not statistically significant so that it can be considered as 1:1).

There seems no reason to doubt that prior to 1940 the ratio of the incidence of coronary arteriosclerosis and acute myocardial infarction among White individuals was actually at least 2 males to 1 female. Evidence from all sources, including the Barnes autopsy series, supports this conclusion. Data based on at least 12,000 autopsies on White adults from three centers (St. Louis, New Orleans, Rochester) indicate that since 1940 the ratio of incidence of acute myocardial infarction in the two sexes is 1:1. Information is needed from numerous other sources before definite conclusions are drawn. However, in view of the large sample that already has been analyzed, it seems unlikely that further studies of autopsies will alter the results significantly.

According to all classical studies the incidence of acute myocardial infarction is far greater among young White men than among young White women and this disproportion decreases with increasing age and finally disappears. The relative incidence in the two sexes in the Barnes autopsy series follows this general pattern and differs only in degree. In both periods (1910 to 1939 and 1940 to 1954) the incidence of acute myocardial infarction was significantly greater in men than in women in the younger age-groups. Among the older age-groups in the period 1910 to 1939, the incidence in the two sexes was similar. However, among the older age-groups in the period 1940 to 1954 the incidence of acute myocardial infarction was higher in women than in men. Thus in the recent period the incidence was higher in young men than in young women but higher in old women than in old men and the resulting overall ratio was 1:1.

The entire autopsy series was divided into age-groups for each sex (40 to 49, 50 to 59, and so on) and the incidence of acute myocardial infarction was determined in each age-group. Since the percentage incidence of acute myocardial infarction among old women was much greater in the period 1940 to 1954 than in the preceding period, it is apparent that the changing sex ratio is due, at least in part, to a disproportionate rise in the incidence of acute myocardial infarction among old women and not simply to either an absolute or relative increase in the number of old women in the autopsy series.

The relative incidence of acute myocardial infarction in the two sexes among autopsied White individuals in New Orleans was similar to that in the corresponding age-groups at Barnes Hospital. Information related to this feature is not yet available from the autopsy series at the Mayo Clinic.
No evidence was found to indicate that the changing sex ratio of acute myocardial infarction could be accounted for by a changing incidence of diabetes mellitus, hypertension, or obesity. However, it should be pointed out that in both periods (1910 to 1939 and 1940 to 1954) the relative incidence of acute myocardial infarction in the two sexes was different among diabetic patients than among non-diabetic patients (among diabetic patients before 1940 the sex ratio for acute myocardial infarction was 1:1, but after 1940 there was a preponderance of women; among non-diabetic patients before 1940 the sex ratio was 2.3 women to 1 man and after 1940 it was 1.4:1). Although a change has occurred in the relative sex incidence among diabetic patients and non-diabetic patients, acute myocardial infarction is still slightly more common among male non-diabetic patients than among female non-diabetic patients and it is slightly more common among female diabetic patients than among male diabetic patients.

Most studies in the United States and Africa have indicated that the incidence of acute myocardial infarction is lower among Negroes than among Whites. The pathologists at Washington University wanted to determine whether or not changes in incidence had occurred among Negroes similar to those changes among Whites. Since the autopsy series from Barnes Hospital consists largely of White individuals it was necessary to examine others. The Negro components of autopsy series from 4 hospitals were analyzed with the cooperation of Drs. J. O. Blache, R. S. Jason, R. L. Holman, and H. C. McGill, Jr. These hospitals were Barnes, Charity of Louisiana in New Orleans, Howard University in Washington D. C., and Homer G. Phillips in St. Louis. Approximately 8,000 autopsies performed on adult Negroes between 1910 and 1954 were analyzed and compared with approximately 10,000 autopsies performed on adult Whites from St. Louis and New Orleans.

The overall incidence of acute myocardial infarction was 5 times as high among the Whites as among Negroes. The difference was much greater in the period 1940 to 1954 than in the period 1910 to 1939 because the incidence among White individuals had risen tremendously but that among Negroes had risen only slightly. The difference in incidence increased with increasing age because the incidence rose sharply among Whites with increasing age but showed little change among Negroes. The increasing difference in the incidence of acute myocardial infarction with increasing age is not simply a matter of difference in longevity, because the data on incidence refer to the percentage incidence among those who survive to a given age. For example, more than 25% of a group of White women who reached the age of 70 died of myocardial infarction and the corresponding figure for a group of Negro women over 70 years old was only 2%. The incidence of acute myocardial infarction among Negroes was similar in the two sexes in both periods that were studied.

Information from all available sources indicates a rising incidence of acute myocardial infarction among White individuals in the United States and the data from the autopsies studied by the group at Washington University tend to confirm this rise. The overall incidence of acute myocardial infarction among the Barnes autopsies was 29 times as high in the decade 1945 to 1954 as it was in the decade 1910 to 1919. The rise occurred in all age-groups of both sexes and was not simply a result of an ageing population. No evidence was found to indicate that the rise in incidence could be accounted for by a rise in the incidence of diabetes mellitus, hypertension, and obesity. It seems likely that some changing factor(s) in our civilization is responsible and it is remarkable that its effect has been almost exclusively confined to members of the White race.

Many investigators have noted a close association between diabetes mellitus and coronary heart disease. The Washington
University group found that acute myocardial infarction was 4 times more common among autopsied White diabetic patients than among autopsied White non-diabetic patients. However, among Negro diabetic patients, acute myocardial infarction was not significantly more common than among non-diabetic patients. Thus a Negro diabetic patient is even less likely to die of myocardial infarction than a non-diabetic White patient. It is interesting to note that diabetic patients with acute myocardial infarction did not die at an earlier age than non-diabetic patients.

Many observers have thought that coronary heart disease was more common among overweight individuals than among those of normal weight or less. However, some recent reports have appeared suggesting that this relationship has not been proved, at least in certain age-groups. S. M. Garn, M. M. Gertler, S. A. Levine, and P. D. White (Ann. Int. Med. 34, 1416 (1951)) found no connection between body weight and myocardial infarction in young men. Terminal weights were available for most of the Barnes autopsies in all age-groups. Several comparative groups were established but no connection between the terminal body weight and the incidence of acute myocardial infarction was demonstrated in any age-group. Furthermore, no evidence was found to indicate that weight loss had been a prominent feature in the patients with acute myocardial infarction.

Most investigators have postulated a close association between coronary heart disease and hypertension. However, some recent workers including L. H. Sigler (Ann. Int. Med. 42, 369 (1955)) have suggested that the association may be merely the chance association of 2 common diseases. The Washington University group used the average weight of the kidneys of the patients with acute myocardial infarction as a rough guide to the degree of hypertension during life. The average weight of the kidneys of the patients with acute myocardial infarction was less than that among patients with "normal" kidneys and more than that among patients that died directly from hypertension. However, there was no significant difference in the average weight of kidneys of patients who died of cancer and those who died of acute myocardial infarction. Thus, with this crude test, the investigators at Washington University were unable to demonstrate any greater association between acute myocardial infarction and hypertension than between carcinoma and hypertension.

The data obtained from autopsy series by the Washington University group confirm some widely held views regarding acute myocardial infarction but do not confirm others. The facts regarding the incidence of acute myocardial infarction among 17,000 autopsies that are the most interesting are: (1) the discovery that a change has occurred in the relative incidence of the disease in White individuals of the two sexes from 2:1 (males:females) before 1940 to 1:1 since 1940; (2) the discovery that the incidence in older White women has increased more since 1940 than in other age-sex-groups; (3) the discovery that the difference between the incidence in Negroes and Whites is increasing rather than decreasing; (4) the discovery that diabetes mellitus did not have a significant effect on the incidence in Negroes although diabetes mellitus unquestionably has a profound effect on the incidence of acute myocardial infarction among White individuals.

Many other studies must be made before the full significance of these data are known. The Washington University pathologists state that even in their own hospital the clinical diagnosis of acute myocardial infarction was made more often in men than women during the same period in which the incidence was 1:1 in the two sexes among autopsies. It seems imperative that clinical material be carefully re-evaluated before final conclusions are drawn. Another aspect that must be explored further is the effect of race. The differences in the incidence of acute myocardial infarction among Negroes...
ELECTROLYTE METABOLISM IN KWASHIORKOR

The syndrome of kwashiorkor is under active investigation in many parts of the world and from many points of view (Nutrition Reviews 13, 67 (1955)). Among the most prominent abnormalities present in this disease are the gross disturbances in water, electrolyte, and protein metabolism manifest clinically in nearly every case by edema and hypoalbuminemia. An investigation of the electrolyte disturbance in patients having kwashiorkor, and its relationship to nitrogen balance, has recently appeared (J. D. L. Hansen, South African J. of Lab. and Clin. Med. 2, 206 (1956)).

Seven males with edema, hypoalbuminemia, a history of a post-weaning diet, and with recent diarrhea, were studied by a balance technique including separate collection of urine and feces. The first 2 patients were treated with diets consisting of milk with a supplement of potassium acetate. Cumulative balances, which are presented in detail in the study, showed an initial small retention of sodium and a gain in weight, followed by a considerable negative balance accompanying the loss of edema. Potassium and nitrogen were retained throughout the experiment, with maximal uptake of potassium in the first 3 days at a potassium to nitrogen diet ratio that greatly exceeded 3 mEq per gram. Following this initial period the ratio between potassium and nitrogen uptake approximated 3 mEq per gram (the ratio of these elements in muscle). It was noted that there was considerable diuresis and loss of edema before a significant rise in the serum proteins took place.

The subsequent 5 cases were placed on nitrogen-free diets for four to seven days to investigate the effect on the edema of supplying only electrolytes and carbohydrates. In these cases potassium retention was maximal in the first two or three days, at a time when the infants were consistently in negative nitrogen balance. Following introduction of nitrogen into the diet, potassium retention paralleled that of nitrogen. Actual retentions of potassium on the nitrogen-free regimens varied between 3.18 and 9.9 mEq per kilogram of body weight, a degree of depletion approximating that seen in severe infant diarrhea.

The initial period of sodium retention was of variable duration, being as long as six to eight days in 2 cases. The sodium diuresis was not necessarily dependent upon the protein intake, although in 2 cases the sodium diuresis and loss of edema occurred only following the introduction of milk feedings. In one case there was a suggestion that a positive potassium balance was essential for the continuation of the sodium diuresis. Nitrogen was retained by all of the patients in amounts somewhat larger than the retentions in 2 well-nourished control patients of the same ages. The sodium, potassium, and chloride concentrations in the serum were measured at intervals during the studies. The pre-treatment sodium and chloride levels showed a wide scatter within the accepted normal range with little, if any, shift during treatment. The pre-treatment concentrations of serum potassium were significantly depressed and rose to normal levels in conjunction with potassium repletion.

These balance studies are interpreted by Hansen to suggest an absolute and relative potassium deficiency in these cases.