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Number 152

Serum Uric Acid Values Of Youths 12-17 Years

United States

Serum uric acid values are presented and discussed by age, sex, race, and socioeconomic level of youths 12-17 years of age in the United States, 1966-70.

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Under the legislation establishing the National Health Survey, the Public Health Service is authorized to use, insofar as possible, the services or facilities of other Federal, State, or private agencies.

In accordance with specifications established by the National Center for Health Statistics, the Bureau of the Census, under a contractual arrangement, participated in planning the survey and collecting the data.

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SERUM URIC ACID VALUES
OF YOUTHS 12-17 YEARS

Paul S. Levy, Sc.D., Peter V. V. Hamill, M.D., M.P.H., Felix Heald, M.D., and Michael Rowland[a]

INTRODUCTION

This report of serum uric acid values as determined from blood samples of youths 12-17 years of age in the United States is one of a series of reports presenting findings from Cycle III of the Health Examination Survey (HES). The means and selected percentiles of the serum uric acid values are examined here by sex, age, race, family income, education, and geographic location in the United States. As described in a detailed report of its general plan and operation,[1] the Health Examination Survey is conducted in a succession of cycles.

Cycle I of the HES, conducted from 1959 to 1962, obtained information on the prevalence of certain chronic diseases and on the distribution of a number of anthropometric and sensory characteristics in the civilian, noninstitutionalized population of the continental United States aged 18-79 years. The detailed plan of Cycle I has been described,[2] and most of the results are published in other reports in Series 11 of *Vital and Health Statistics.*

Cycle II of the HES, conducted from July 1963 to December 1965, involved selection and examination of a probability sample of noninstitutionalized U.S. children aged 6-11 years. This program succeeded in examining 96 percent of the 7,417 children selected for the sample. The examination had two focuses: (1) factors related to healthy growth and development as determined by a physician, a nurse, a dentist, and a psychologist and (2) a variety of somatic and physiologic measurements performed by specially trained technicians. The detailed plan and operation of Cycle II and the response results are described in *Vital and Health Statistics,* Series 1-Number 5.[3]

HES Cycle III, conducted from March 1966 to March 1970, was essentially an agewise extension of Cycle II into adolescence. As described in detail in "Plan and Operation of a Health Examination Survey of U.S. Youths, 12-17 Years of Age,"[4] Cycle III was more similar to Cycle II than to Cycle I not only in form, content, and style but also in having its major emphasis on factors of "normal" growth and development rather than on chronic diseases. These analyses on "normal" growth and development of adolescents have been well underway since 1970, and some of the results from the battery of body measurements have already been published,[5-7] as have the initial results of the hematocrit findings.[8]

The present report of uric acid values is the second in the series presenting findings from the sample of blood drawn from each youth. No blood specimens were obtained from the children in Cycle II, but specimens were obtained from the adults in Cycle I.

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The information from the analysis of blood is intended for use as much needed reference data both for clinical and for epidemiologic estimates of variation in a well-defined population. It also enables examination of another aspect of growth and development during adolescence. The procedure by which the Division of Health Examination Statistics obtained advice on the selection of the analyses to be made on the blood specimens and the cooperative arrangements which were subsequently made with the Clinical Chemistry and Hematology Branch (now Clinical Chemistry Division) of the Center for Disease Control (CDC) have been described elsewhere.[4]

The authors and the Division of Health Examination Statistics are grateful for the technical advice given by Dr. Gerald Cooper and Dr. Alan Mather and for their administrative assistance in arranging the laboratory determinations that were performed by the Clinical Chemistry and Hematology Branch, and to Mrs. Margie Sailors for coordination and verification of the laboratory data and its transmission.

METHOD

At each of 40 preselected locations (see appendix I for sample design) throughout the United States, the youths were brought to the centrally located mobile examination center for an examination that lasted about 3½ hours. Six youths were examined in the morning and six in the afternoon. Except during vacations, they were transported to and from school and/or home.

When the youths entered the examination center, their oral temperatures were taken, and a cursory screening for acute illness was made; if illness was detected, the youth was sent home and reexamined later. The examinees changed into gymnasium-type shorts; cotton sweat socks; a terry-cloth robe; and, for the girls, a light, sleeveless topper. All six then proceeded to different stages of the examination, each one following a different route. The 3½-hour examination was divided into six 35-minute time periods, each consisting of one or more detailed examinations at a designated station. At the end of each period, the youths rotated to other stations, so that at the end of 3½ hours each youth had been given essentially the same examinations by the same examiners, but in a different sequence. Four of these examination time periods were allocated to examinations by a pediatrician, a dentist, and a psychologist,[b] and the other two were allocated to a group of examinations performed by highly trained technicians. This last group of examinations consisted of X-rays of the chest and hand-wrist, hearing and vision tests, measures of respiratory function, a 12-lead electrocardiogram, a submaximal exercise tolerance test on a treadmill with chest leads to a continuous electrocardiogram, a battery of body measurements, grip strength measurements, examination of blood and (on girls only) urine cultures for bacteria, and a privately administered health behavior and attitude questionnaire.

Blood Specimen and Serum Uric Acid Determination

The analyses for serum uric acid were performed for the Health Examination Survey by the Clinical Chemistry and Hematology Branch of the Center for Disease Control, Public Health Service, Atlanta, Ga. They employed an automated colorimetric phosphotungstic acid procedure on the Technicon AutoAnalyzer-I using the N-13b method.[c] The assays were controlled by a manual reference (Brown) method, and the automated results were originally validated against a uricase assay. The importance of specifying the type of laboratory method employed is emphasized in the discussion section, and the technical details of the method are presented in both the discussion and appendix III.

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[b]The entire examination by the psychologists consisted of two consecutive time periods (70 minutes). Two psychologists performed identical examinations simultaneously at separate stations.

[c]Procedure N-13b, Technicon Laboratory Method File, 1965, Technicon Instruments Corp., Tarrytown, N.Y.

The development of the technique used by the HES for obtaining and processing the blood specimen is also described in appendix III. As described in the hematocrit report,[8] the microhematocrit was the only complete laboratory determination performed on the blood specimen directly in the examination trailers. The bulk of each blood specimen, after preliminary laboratory preparation, was properly separated into its various subsamples and packed into specially devised styrofoam containers for shipment via air freight to either the Immunogenetics Laboratory of The Johns Hopkins University, Baltimore, Md., or the CDC in Atlanta, Ga.

Frozen serum for the three blood chemistries—uric acid, total serum cholesterol, and protein bound iodine (PBI)—was shipped to the Clinical Chemistry Section of CDC. Within a day after arrival at CDC (or at the most within two days), serum for uric acid was thawed, determinations were promptly made, and the aliquots for the other two chemical analyses were sent to the appropriate laboratory. A specimen of clotted blood was sent directly to the Venereal Disease Research Laboratory (CDC) for analysis.

Race

Race was recorded as "white," "Negro," and "other races"[d] (see appendix II). In Cycle III, white youths constituted 84.74 percent of the total youths examined; Negro youths, 14.76 percent; and youths of other races, only 0.50 percent. In Cycle II, white children constituted 85.69 percent of the examined subjects and Negro children, 13.86 percent. (The differential response rate by age, sex, and race is analyzed and discussed in appendix I. The increased proportion of Negro subjects in Cycle III was due to their better response rate—the overall Negro response rate was 96.6 percent and the overall white response rate was 89.1 percent.) As in Cycle II, because so few youths of "other races" were part of the sample, data for them have not been analyzed as a separate category. Whenever data are analyzed independently of a classification by race, however, data for these youths are included.

[d]The same classification scheme as used in the 1960 census was employed here. As described in the previously mentioned report on the operation of HES Cycle III,[4] this information was obtained at the initial household interview by the U.S. Bureau of the Census fieldworker. The accuracy of the information was checked at the subsequent home visit by the highly experienced representative from HES and again at the examination in the trailer. A final record check by birth certificate turned up only seven inconsistencies, and these were mostly pertaining to the category "other races." Hence, the possible extent of misclassification of the race variable, as described, is so minimal that it could have no effect on the data analyzed in this report. However, when comparing the present HES findings to those of other variously defined racial groupings in the world, the degrees of genetic admixture, as first discussed by Herskowitz[9] in 1928 and later by Glass and Li,[10] by Roberts,[11,12] and by Reed,[13] should be taken into consideration.

RESULTS

Age and Sex

The estimated number and percent distribution of male and female youths 12-17 years of age in each of 19 uric acid groups are shown in tables 1 and 2, respectively. The patterns shown in these distributions are discussed below in terms of a few summary statistics.

The estimated mean uric acid levels for each of 12 age-sex classes are shown in table 3 and figure 1. Among male youths 12-17 years of age, mean uric acid levels increased with age from a low of 4.4 mg/100 ml in 12-year-olds to a high of 5.9 mg/100 ml in 16- and 17-year old males. Differences in mean uric acid levels between males in consecutive age groups were greatest at the youngest ages and decreased consistently with increase in age, from a difference of 0.6 mg/100 ml in the mean uric acid level of 13-year-olds and that of 12-year-olds to no difference in the mean level of 16- and 17-year-old males. In female youths, on the other hand, mean uric acid levels were in the 4.6-4.7 mg/100 ml range, with no significant differences observed among the six age groups. With the exception of 12-year-olds, males in each age group showed higher mean uric acid levels than their female counterparts.

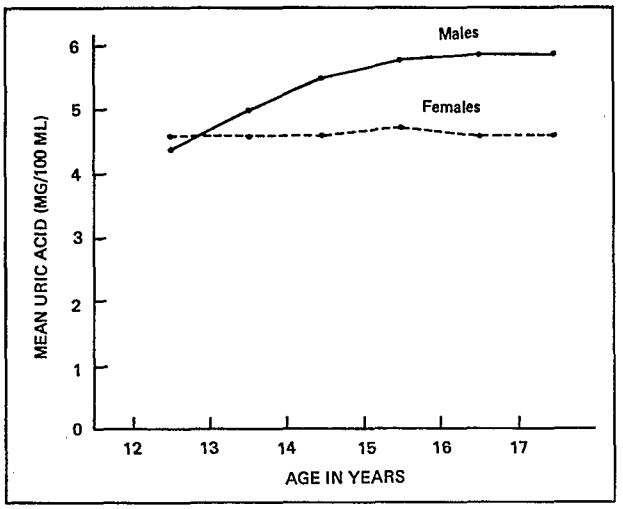

Figure 1. Mean uric acid levels for youths 12-17 years of age, by age and sex: United States, 1966-70.

Estimated percentiles of the uric acid distributions are shown by age for male and female youths in table 3 and figures 2 and 3. For each age-sex group the median and mean were almost identical, which indicates symmetry of the distribution about the mean. The pattern of increased mean uric acid levels with increased age shown above for male youths also occurred at the two extremes of the distribution, namely the 5th and 95th percentiles (table 3). At the low end of the distribution, the 5th percentile for 12-year-old males was 2.7 mg/100 ml, but it increased to a high of 4.2 mg/100 ml (an increase of 1.5 mg/100 ml) for 17-year-old males, with the biggest differences between consecutive age groups occurring among the younger adolescents. For females, the 5th percentile varied only slightly among the six age groups within the range of 2.9-3.2 mg/100 ml, with no consistent increase or decrease with age. With the exception of 12-year-olds, the 5th percentile of the uric acid distribution was consistently higher for males than for females, with differences between the sexes being greater for the older youths. At the upper end of the distribution, namely the 95th percentile, a similar pattern occurred for both males and females. For males, the 95th percentile showed an increase with age from a low of 6.4 mg/100 ml for 12-year-olds to an approximate average of

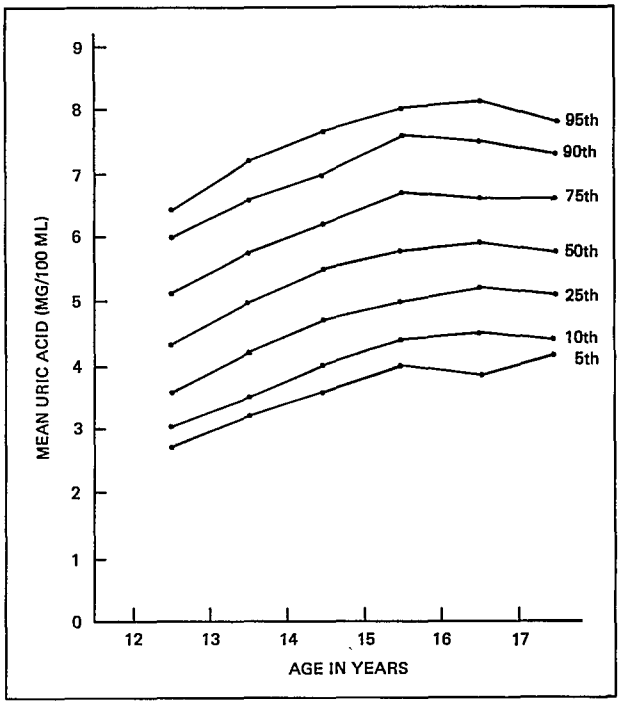

Figure 2. Selected estimated percentiles of the uric acid distribution in males, by age and sex: United States, 1966-70.

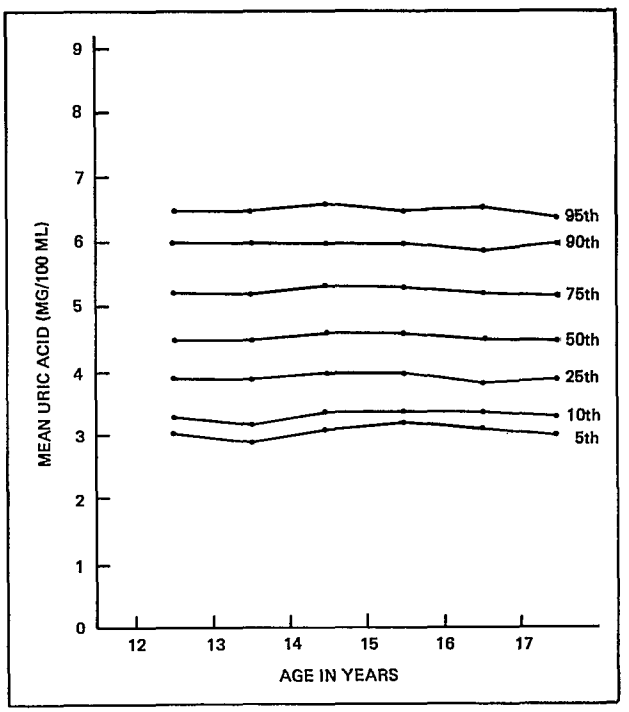

Figure 3. Selected estimated percentiles of the uric acid distribution in females, by age: United States, 1966-70.

8.0 mg/100 ml for 15- to 17-year-olds (an increase of about 1.6 mg/100 ml), with the sharpest differences between consecutive age groups occurring among the younger age groups. In contrast, among females the 95th percentile showed little or no change with age, staying in the 6.4-6.6 mg/100 ml range over all age groups. Again, beginning with age 13, the 95th percentile was higher at each age group for males than for females. In general, the percentiles discussed above, when plotted against age, were remarkably parallel for both males and females (figures 2 and 3).

Mean uric acid levels for each age-sex group are plotted against the percentile distribution of the opposite sex in figures 4 and 5. Males fall just short of the 50th percentile for females at age 12. On the average, the levels for males continue to rise relative to those of females of similar chronologic age until the mean reaches the 90th percentile for females at ages 16 and 17. Conversely, mean uric acid levels in females fall from just above the 50th percentile for

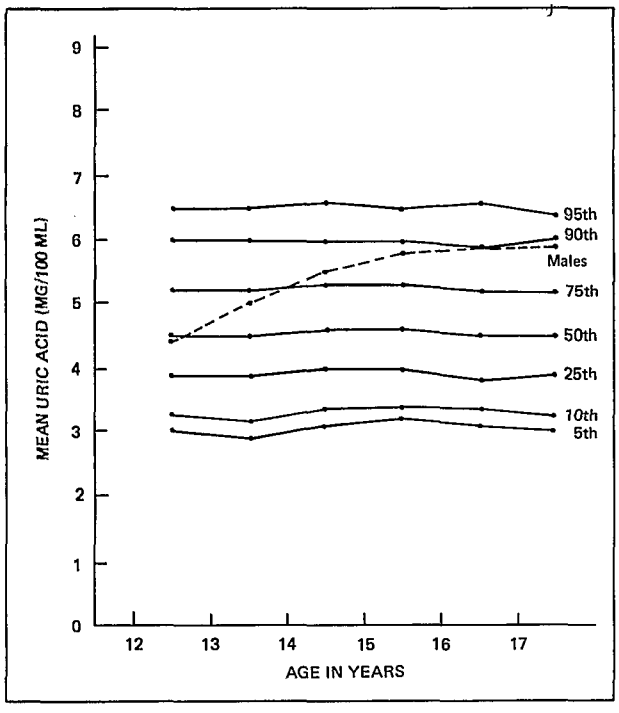

Figure 4. Mean uric acid levels of males 12-17 years of age, plotted on the percentile distribution of females: United States, 1966-70.

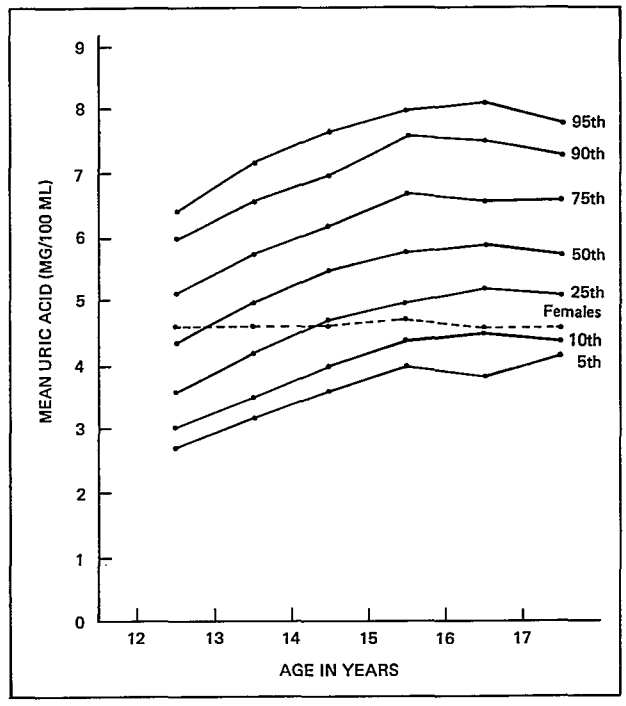

Figure 5. Mean uric acid levels of females 12-17 years of age, plotted on the percentile distribution of males: United States, 1966-70.

males at age 12 to just above the 10th percentile for males at ages 16 and 17.

Age, Sex, and Race

The estimated number of white and Negro youths in each of 19 uric acid groups is shown in tables 4 and 5 and equivalently as a percentage distribution in tables 6 and 7. The patterns observed in these distributions are discussed below.

Mean uric acid levels are shown by age for white and Negro males and females (table 8 and figure 6). In each of the six age groups, white males had higher mean uric acid levels than Negro males of the same age group, and white females had higher mean uric acid levels than Negro females of the same age group. The average difference over all age groups in mean uric acid levels of white youths and those of Negro youths of the same age group was about 0.6 mg/100 ml in males and about 0.5 mg/100 ml in females. The increase with age in mean

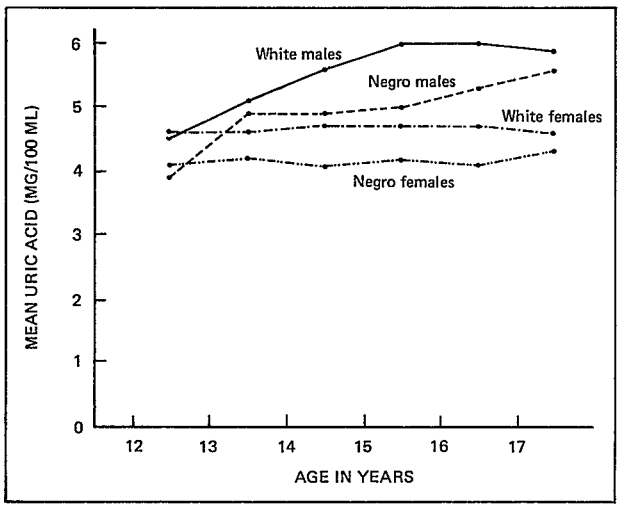

Figure 6. Mean uric acid levels of youths 12-17 years of age, by age, race, and sex: United States, 1966-70.

uric acid levels shown above for the total population of male youths occurred separately in white males and in Negro males. In white males, however, the increase with age in mean uric acid leveled off after age 15, whereas in Negro males, the increase with age seemed to continue through age 17. On the other hand, the lack of increase with age in mean uric acid levels shown previously for the total population of female youths was also apparent when white and Negro females were examined separately.

Selected percentiles of uric acid levels are shown for white and Negro youths by age and sex in table 8, and figures 7-10. In general, the differences between white and Negro youths discussed above for the mean of the distribution were also observed at about the same order of magnitude for the lower end of the distribution (5th, 10th, and 25th percentiles), for the median, and for the upper end of the distribution (75th, 90th, and 95th percentiles).

The percentage of white and Negro youths having uric acid levels above 7.9 mg/100 ml, 8.4 mg/100 ml, and 8.9 mg/100 ml is shown in table 9. For each of the six age groups, the proportion of males with levels above 7.9 mg/100 ml and 8.4 mg/100 ml was greater among white than among Negro youths. Likewise, except for 16-year-olds, a higher proportion of white males

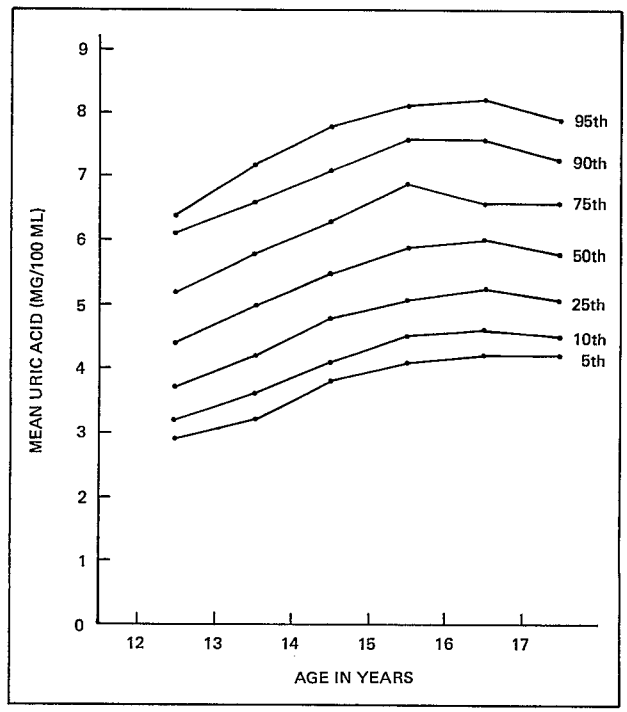

Figure 7. Selected estimated percentiles of the uric acid distribution in white males, by age: United States, 1966-70.

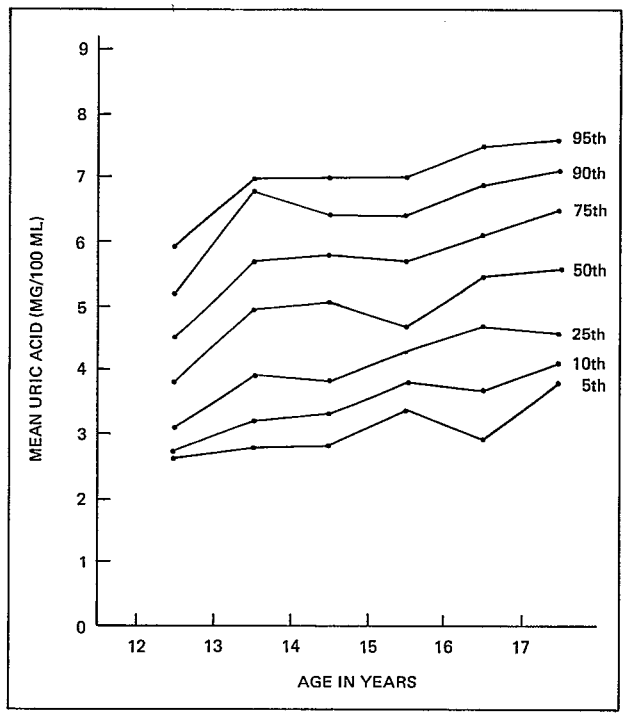

Figure 8. Selected estimated percentiles of the uric acid distribution in Negro males, by age: United States, 1966-70.

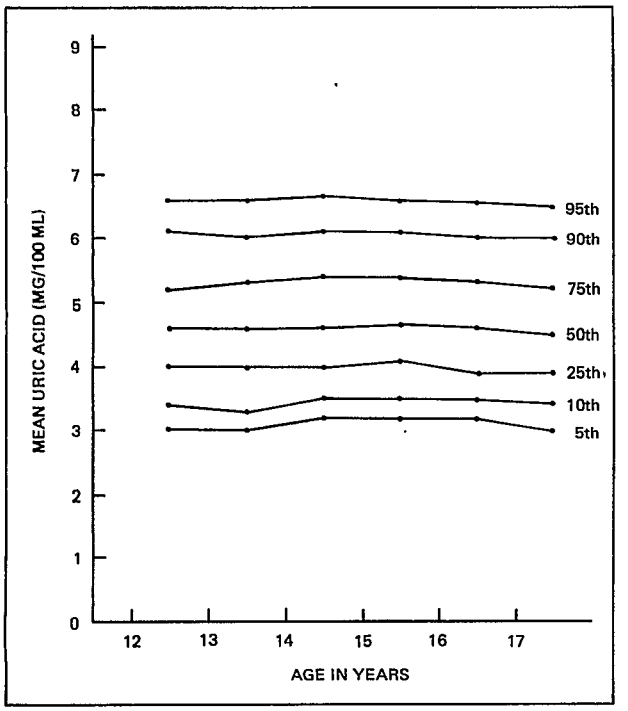

Figure 9. Selected estimated percentiles of the uric acid distribution in white females, by age: United States, 1966-70.

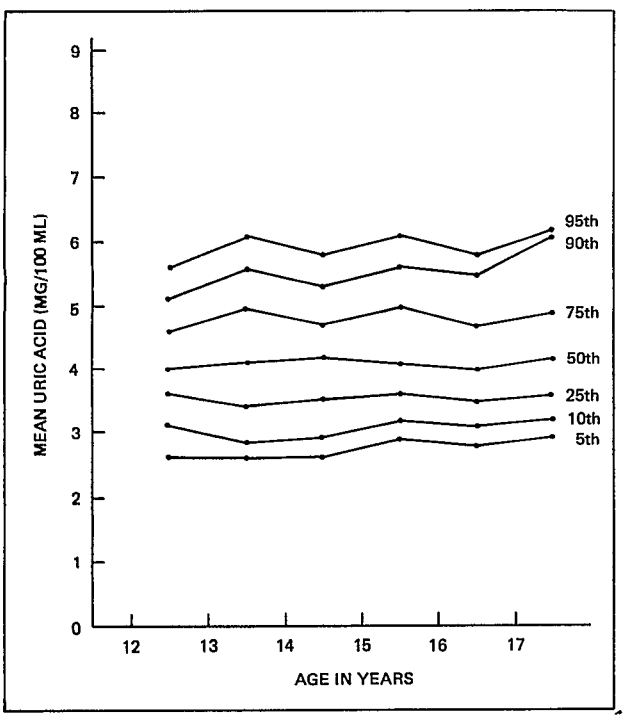

Figure 10. Selected estimated percentiles of the uric acid distribution in Negro females, by age: United States, 1966-70.

than of Negro males had uric acid levels above 8.9 mg/100 ml. In the Negro female group, there were no persons with levels above 7.9 mg/100 ml, whereas for white females, each of the six age groups had some persons with uric acid levels above 7.9 mg/100 ml.

Annual Family Income, Education of Parent, Age, and Sex

Mean uric acid levels are shown by sex, age, and annual family income in table 10 and figure 11. Few, if any, differences were found in mean uric acid levels between the subgroups having low or moderate family income and those having relatively high family income. Similar results were found when the data were examined in terms of sex, age, and education of parent (table 11 and figure 12). Likewise, when the six age groups were combined for white and Negro females, uric acid levels of white females were higher than those of Negro females, regardless of annual family income or education of parent (table 12).

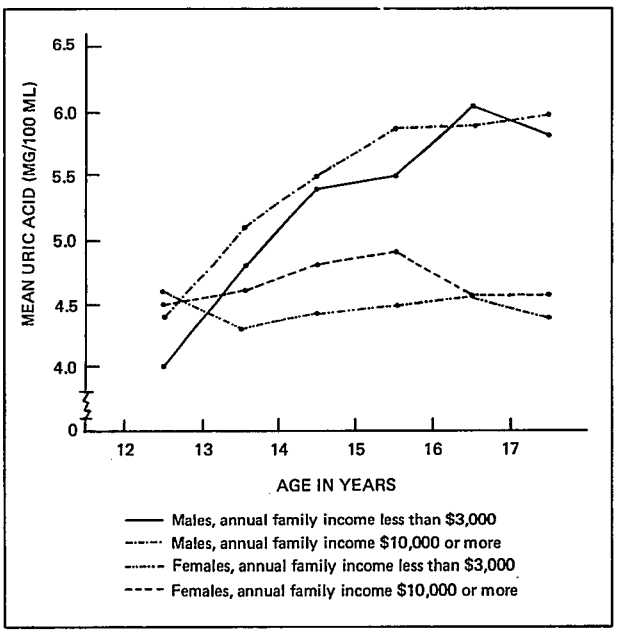

Figure 11. Mean uric acid levels for youths 12-17 years of age, by annual family income, age, and sex: United States, 1966-70.

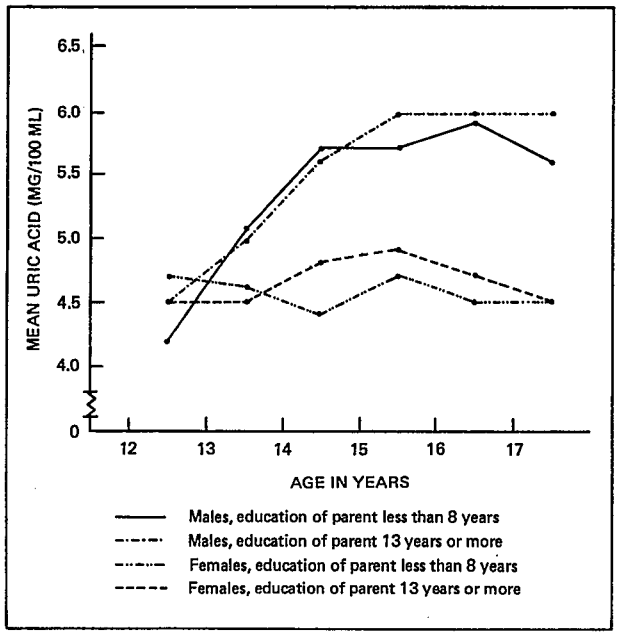

Figure 12. Mean uric acid levels for youths 12-17 years of age, by education of parent, age, and sex: United States, 1966-70.

Place of Residence, Age, and Sex

Mean uric acid levels are shown for white males and females by place of residence (table 13). Mean serum uric acid levels were highest among those residing in rural farm areas, with differences being more pronounced for white males than for white females.

DISCUSSION

In the interpretation of uric acid levels obtained in any study, the laboratory method used is extremely important, as summarized by Wyngaarden.[14] In general, these procedures can be classified as either colorimetric or enzymatic spectrophotometric (uricase). The colorimetric methods are based on the principle that a blue color results from the chemical reaction of uric acid with (usually) phosphotungstic acid, and that the intensity of this blue color is proportional to the amount of uric acid in the sample. The enzymatic method, on the other hand, uses the ultraviolet light-absorbing property of uric acid. In this procedure, the amount of ultraviolet light absorbed by a particular serum sample is measured before and after addition of the enzyme uricase which converts uric acid to allantoin. The difference in absorption is proportional to the concentration of uric acid in the sample, and the concentration is measured by comparison with a calibrated standard.

Since a uricase method is both more specific and potentially more accurate, it is generally more accepted as the reference. On the other hand, it is a more costly and time-consuming laboratory procedure; therefore investigators using other methods should demonstrate the relationship of their method to a uricase method. The colorimetric method used in determining HES levels performed by CDC was originally validated against uricase assays and produced values that averaged about 0.5 mg/100 ml higher. Therefore, when the HES data are compared with data from Tecumseh, Mich.,[15] which were determined by a uricase method (table 14), 0.5 mg/100 ml was subtracted from the HES mean values as the most reasonable adjustment.

There are many variables that influence uric acid values in healthy individuals. First of all, as already discussed, the laboratory technique used is extremely important in the interpretation of uric acid determinations.[16,17] Likewise, a small diurnal variation has been reported, with highest levels occurring in midafternoon.[18] HES findings, however, showed no differences between the mean uric acid levels of those youths examined in the morning and those examined in the afternoon. Several studies have found a positive association between uric acid and body size variables such as weight, relative weight, surface area of the body, and ponderal index and somatotype.[16,19,20,22] In almost every study in which both male and female subjects of comparable age have been used, it was found that postpubertal uric acid levels were higher in males than in females.[15,23-27] Some studies have shown that mean uric acid levels in males remain relatively stable during adult life, and

that female mean values, after remaining stable throughout the childbearing years, increase at the time of menopause.[15,26,28] In a study by Zalokar et al.[20] of over 6,000 healthy male subjects, the positive relationship between age and uric acid levels noted above disappeared when the data were adjusted for percent body fat, and, in fact, a negative relationship was found between age and uric acid when the data were so adjusted. HES findings on the relationship between uric acid levels and such variables as height, weight, and hematocrit will be discussed in a future report.

Genetic and Environmental Factors

The relative influence of genetic and environmental factors on uric acid levels has been investigated. A study by Boyle et al.[29] of 51 monozygotic twin pairs (16 male, 35 female) and 61 dizygotic twin pairs (11 male, 20 female, and 30 of unlike sex) revealed that the intrapair variance in uric acid levels among female dizygotic twin pairs was significantly higher than those among monozygotic female twin pairs. In contrast, no significant difference was found between the intrapair variance among male dizygotic twin pairs and that among male monozygotic pairs. From this they concluded that a fairly strong genetic influence on uric acid level exists in females, but probably not in males. An additional finding of this twin study was that in both the monozygotic and dizygotic female twin pairs, the intrapair variance among those twins living apart for more than a year was greater than that found among those living together in the same household, and from this they concluded that environmental as well as genetic factors act as determinants of uric acid levels.[29] An earlier study by Jensen et al.[30] of a smaller number of twin pairs also showed significantly greater intrapair variation in uric acid levels among the dizygotic than among the monozygotic pairs, but these results were not analyzed separately by sex. Like the Boyle et al. study,[29] other studies on familial aggregation of uric acid levels have shown evidence of stronger genetic determination in females than in males.[31,32]

While several studies have shown racial differences in uric acid levels, the findings have not been consistent over different studies. For example, Ford and DeMos,[33] in a survey of 200 healthy Caucasian males, 100 healthy Chinese males, and 237 healthy Haida Indian males, showed that the Chinese males had significantly higher mean uric acid levels than the Caucasians and Haida Indians. On the other hand, Duff et al.[27] found that although urban Chinese from Malaya had high mean serum uric acid levels relative to Caucasians from Tecumseh, Mich., Chinese from Taiwan had lower mean uric acid levels than the Tecumseh Caucasians. A study[34] conducted in Alabama indicated that Negro adult males and females had higher uric acid levels than Caucasians, a finding which differs from those of HES for the adolescent age group.

While association between serum uric acid levels and certain socioeconomic variables has been found by some investigators but not by others,[23,26,35,36] perhaps the most curious finding from epidemiologic studies of uric acid is the association between uric acid levels and such psychosocial variables as drive, achievement, and leadership.[21,35,37-39] In a much quoted study, Dunn and his coworkers[21] found that executives had higher uric acid levels than craftsmen. Likewise, Kasl and his coworkers,[35,38] in a study of teenage males, found a strong association between serum urate levels and high school grade point average, college attendance, and extracurricular and social activities. At the same time, no association was found between uric acid levels and either education of parent or family income, in accordance with similar HES findings. On the basis of such evidence, Kasl et al.[35,37,38] present a case for the role of uric acid as a cortical stimulant inducing achievement.

Age and Sex Differences

The increase with age in the mean uric acid levels of male youths from age 12 to age 15 is a

striking finding of this survey. There was a 14-percent increase in mean uric acid levels between 12- and 13-year-olds, a 10-percent increase between 13- and 14-year-olds, and a 5-percent increase between 14- and 15-year-olds. Thus, in a period of 3 years, mean uric acid levels increased from 4.4 mg/100 ml in 12-year-old males to 5.8 mg/100 ml in 15-year-old males (an increase of 32 percent).

There were no differences observed among the older adolescent males, i.e., those aged 15, 16, and 17 years. Some insight into whether most adolescent males 15-17 years of age have reached their adult uric acid levels comes from comparing the levels obtained by HES for males aged 15-17 years with those obtained for young adults by other investigators. Findings by Zalokar[20,40] in a study of Parisian male civil servants showed mean uric acid levels of 5.8-5.9 mg/100 ml in young adults aged 20-29 on the basis of colorimetric determinations (the same as those used for the HES data). The Tecumseh study, using the uricase enzymatic method, showed mean levels of 5.39 mg/100 ml in young males 20-29 years of age.[15] However, since the colorimetric method used in HES data produces values approximately 0.5 mg/100 ml higher than those produced by uricase assays, adjustment of the Tecumseh findings for males aged 20-29 years would bring them in line with HES findings for males aged 15-17 years. Thus, on the basis of these comparisons, there seems to be substantial evidence that adult uric acid levels are reached in most males as early as 15 years of age. In the Metropolitan Life Insurance Co. study of 1,077 male and 1,388 female employees, however, males under 35 had substantially higher mean uric acid levels (6.4 mg/100 ml based on colorimetric determinations) than those obtained by HES for 15- to 17-year-old males.[26] The uric acid levels of males in the Metropolitan Life Insurance study were much higher than those obtained for males elsewhere in the literature, with the exception of those male executives found by Dunn et al.[21] Because the males represented in the Metropolitan Life Insurance data may have included a large proportion of executives, and because executives were shown to have high uric acid levels in at least one study,[21] caution should be exercised in the interpretation of any comparisons involving these male life insurance employees.

In contrast with males, HES female youths showed no increase with age in mean uric acid levels, and only at age 12 were the mean levels higher than those of HES males (4.6 mg/100 ml in 12-year-old females vs. 4.4 mg/100 ml in 12-year-old males). The mean uric acid levels of 4.6-4.7 mg/100 ml obtained by HES for female youths aged 12-17 years were only slightly higher than those of 4.4 mg/100 ml obtained for females under 35 in the Metropolitan Life Insurance study.[26] Females 20-34 years of age in the Tecumseh study[15] had mean uric acid levels of 4.0 mg/100 ml by the uricase method; and if the 0.5 mg/100 ml adjustment were made, it would bring theirs closely in line with the levels obtained by HES for adolescent females. Thus, there is substantial evidence that female adolescents already have uric acid levels that are similar to those of young adult females.

The findings of an increase with age in mean uric acid levels among the HES males but not among the females somewhat resemble HES findings of an increase with age in mean hematocrit among males, but not among females.[8]

Because of the size of the sample on which they are based and because this is a probability sample chosen to be representative of U.S. youths 12-17 years of age, the HES data give the best picture at the present time of uric acid levels in adolescent males and females. The only other population study which gives uric acid data in enough detail to compare by age and by sex with the HES findings is the first Tecumseh study, conducted in 1959-60.[15]

As was mentioned above, uric acid levels in the first Tecumseh study were determined by an enzymatic (uricase) assay, whereas HES determinations were made by a colorimetric method which when assayed against uricase gave results that were approximately 0.5 mg/100 ml higher than those obtained with the enzymatic method. Table 14 shows for each age group the mean uric acid levels found in the Tecumseh study alongside the HES uric acid levels, which are reduced

by 0.5 mg/100 ml so as to compare more reasonably with enzymatic determinations of uric acid levels. At almost every age group, the two studies produced means that were very close to each other (sample size for the Tecumseh study adolescents was much smaller than that used for HES, which can account for the fluctuations seen in Tecumseh data when examined by single years of age). As can be seen from table 14, age-sex relationships occurred in Tecumseh data that were similar to those observed in HES, namely an increase with age in male but not in female adolescents.

The Tecumseh study also gives uric acid levels for children 5-9 years of age, and it was found that the mean uric acid levels for children in this age group were approximately the same for boys as for girls (3.63 mg/100 ml for 5- to 9-year-old boys; 3.71 mg/100 ml for 5- to 9-year-old girls) and that these mean serum levels were lower than those found in 12-year-olds.

The large sex difference in serum urate levels which first emerges during adolescence has aroused little interest heretofore. There are no data in the literature which would suggest that differing rates of production of uric acid between boys and girls could account for these differences. There are data, however, on the renal clearance of urates in children who have higher renal clearances than adults.[41] Among adults, women have higher renal clearances than men, a fact which would explain at least some of the sex difference in serum urate levels.[42] Differences in body mass (estimated by body weight, surface area, or ponderal index) have been reported to be important predictors of hyperuricemia.[43] Whether the pubescent differences in body composition are in any way related to the developing differences in serum urates remains to be demonstrated. In similar fashion, the relationship between the endocrine events at pubescence and serum urate levels likewise remains a possibility. This is suggested by the changes at pubescence documented in this report and further suggested by the rise in serum urate levels in women in their late forties or early fifties concurrent with menopause. Although this rise in serum urate level at the time of menopause is well documented, little is known about the relationship between uric acid metabolism and the normally functioning endocrine system.

Race

A remarkably consistent average difference of approximately 0.5 mg/100 ml between mean serum uric acid values of white and Negro youths appeared for both HES males and females. Since these are the only population data on uric acid levels in both Negro and white adolescents comprehensive enough to permit analysis of racial differences, they cannot be related directly to the findings of other studies. As mentioned above, other studies of uric acid levels in several adult populations have shown racial differences, however, these differences have not always been consistent from study to study. Data from a study on Negro and white adult males and females in Alabama showed that Negro males and females had higher uric acid levels than their white counterparts, a finding which contrasts with HES data on adolescents.[34]

Since uric acid determinations were not performed on adults in HES Cycle I, it cannot be determined whether the racial differences for uric acid found in adolescents are also true for adult Americans. Cycle III data also showed that Negro adolescents, both male and female, have lower hematocrits than white youths of comparable age and sex.[8] However, racial differences in hematocrit values were primarily at the lower end of the distribution,[8] whereas differences between uric acid levels of Negro adolescents and those of white adolescents appeared throughout the distribution—i.e., the 5th, 50th, and 95th percentiles.

Place of Residence

The fact that white adolescents from farms had slightly but consistently higher mean uric acid levels than comparable suburban and city residents is an interesting finding and one that cannot be related to other studies. However,

the differences found, although consistent, were small.

Family Income and Education of Parent

Even when standardized for racial differences, no relationship was found between uric acid levels of HES youths and education of parent or family income for either Negro or white persons. Although Acheson[23] found a relationship between uric acid levels and social class in England and also in New Haven, the relationship was weak and was an inverse one, with uric acid levels decreasing slightly with increase in social class. HES data confirm earlier findings by Kasl and his coworkers[38] of a similar lack of relationship between uric acid and education of parent or family income.

Clinical Significance of Uric Acid Levels

Historically, elevated serum uric acid has been of interest particularly because of its association with two extremely painful conditions, gout and renal stones. These conditions, however, rarely occur in adolescence, and their clinical importance to these data would lie in what happens to adolescents with asymptomatic hyperuricemia as the condition accompanies them to adulthood. To our knowledge, there have been no longitudinal studies beginning with adolescents that have dealt with the above question. In adults, the Framingham[28] study followed a population of persons initially aged 30 years and above who were free of gout; after 12 years, gout was found to occur in only 1.1 percent of the persons who initially had uric acid levels under 6.0 mg/100 ml (by the enzymatic method) and in approximately 10 percent of those who initially had levels above 6.0 mg/100 ml. Thus, development of gout seems to be a relatively rare occurrence among persons with asymptomatic hyperuricemia. Other clinical correlates of hyperuricemia are discussed in detail in a recent review article,[16] and will be examined in a subsequent analysis of these HES data.

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LIST OF DETAILED TABLES

Table 1. Estimated number of youths aged 12-17 years in the population, by uric acid groups, sex, and age: United States, 1966-70

Uric acid group	Male						Female					
	12 years	13 years	14 years	15 years	16 years	17 years	12 years	13 years	14 years	15 years	16 years	17 years
	Estimated number of youths in population in thousands											
All groups	2,032	2,006	1,951	1,900	1,836	1,764	1,970	1,946	1,901	1,851	1,789	1,746
Under 1.0 mg percent	–	–	–	–	–	–	–	–	–	–	–	–
1.0-1.4 mg percent	–	–	–	–	4	–	–	–	–	–	–	–
1.5-1.9 mg percent	6	3	–	–	–	–	8	7	3	6	–	2
2.0-2.4 mg percent	43	12	3	–	–	–	29	30	25	19	22	40
2.5-2.9 mg percent	129	42	24	5	32	4	51	86	42	30	41	39
3.0-3.4 mg percent	248	138	48	28	15	21	177	154	161	172	143	152
3.5-3.9 mg percent	389	220	135	56	53	27	272	280	263	234	359	263
4.0-4.4 mg percent	331	289	193	165	73	152	456	405	406	337	300	376
4.5-4.9 mg percent	319	293	267	215	154	208	383	364	351	406	338	290
5.0-5.4 mg percent	218	337	331	311	298	281	259	287	299	277	270	259
5.5-5.9 mg percent	140	244	310	321	341	307	134	139	163	178	145	134
6.0-6.4 mg percent	132	196	267	227	363	284	95	94	84	101	68	107
6.5-6.9 mg percent	41	102	149	194	183	211	73	50	57	36	43	39
7.0-7.4 mg percent	24	62	97	176	141	124	25	29	35	20	33	18
7.5-7.9 mg percent	10	34	62	101	74	74	4	5	7	11	14	11
8.0-8.4 mg percent	3	14	43	56	52	24	4	6	3	7	–	12
8.5-8.9 mg percent	–	10	14	38	35	14	–	4	–	15	5	4
9.0-9.4 mg percent	–	5	3	–	8	21	–	3	–	–	2	–
9.5 mg percent and over	–	5	3	6	11	12	–	6	2	–	4	–

Table 2. Percent distribution of youths aged 12-17 years by uric acid groups, according to sex and age: United States, 1966-70

Uric acid group	Male						Female					
	12 years	13 years	14 years	15 years	16 years	17 years	12 years	13 years	14 years	15 years	16 years	17 years
	Percent distribution											
All groups	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Under 1.0 mg percent .	—	—	—	—	—	—	—	—	—	—	—	—
1.0-1.4 mg percent ..	—	—	—	—	0.2	—	—	—	—	—	—	—
1.5-1.9 mg percent ..	.0.3	0.2	—	—	—	—	0.4	0.3	0.1	0.3	—	0.1
2.0-2.4 mg percent ..	2.1	0.6	0.2	—	—	—	1.5	1.6	1.3	1.0	1.2	2.3
2.5-2.9 mg percent ..	6.4	2.1	1.2	0.3	1.7	0.2	2.6	4.4	2.2	1.6	2.3	2.3
3.0-3.4 mg percent ..	12.2	6.9	2.5	1.5	0.8	1.2	9.0	7.9	8.5	9.3	8.0	8.7
3.5-3.9 mg percent ..	19.1	11.0	6.9	3.0	2.9	1.6	13.8	14.4	13.8	12.6	20.1	15.1
4.0-4.4 mg percent ..	16.3	14.4	9.9	8.7	4.0	8.6	23.2	20.8	21.4	18.2	16.8	21.5
4.5-4.9 mg percent ..	15.7	14.6	13.7	11.3	8.4	11.8	19.5	18.7	18.4	22.0	18.9	16.6
5.0-5.4 mg percent ..	10.7	16.8	17.0	16.4	16.2	16.0	13.1	14.8	15.7	14.9	15.1	14.9
5.5-5.9 mg percent ..	6.9	12.2	15.9	16.9	18.6	17.4	6.8	7.2	8.6	9.6	8.1	7.7
6.0-6.4 mg percent ..	6.5	9.7	13.7	12.0	19.8	16.1	4.8	4.8	4.4	5.5	3.8	6.2
6.5-6.9 mg percent ..	2.0	5.1	7.7	10.2	10.0	11.9	3.7	2.6	3.0	2.0	2.4	2.2
7.0-7.4 mg percent ..	1.2	3.1	5.0	9.2	7.7	7.0	1.3	1.5	1.8	1.1	1.9	1.0
7.5-7.9 mg percent ..	0.5	1.7	3.2	5.3	4.0	4.2	0.2	0.3	0.4	0.6	0.8	0.6
8.0-8.4 mg percent ..	0.1	0.7	2.2	3.0	2.9	1.4	0.2	0.3	0.2	0.4	—	0.7
8.5-8.9 mg percent ..	—	0.5	0.7	2.0	1.9	0.8	—	0.2	—	0.8	0.3	0.2
9.0-9.4 mg percent ..	—	0.3	0.1	—	0.4	1.2	—	0.1	—	—	0.1	—
9.5 mg percent and over	—	0.2	0.2	0.3	0.6	0.7	—	0.3	0.1	—	0.3	—

NOTE: Percents may not add to 100.0 due to rounding.

Table 3. Unweighted and weighted sample sizes, mean uric acid, standard deviation, standard error, and selected percentiles, by sex and age: United States, 1966-70

Sex and age	n	N	$\bar{X}$	s_X	$s_{\bar{X}}$	Percentile						
						5	10	25	50	75	90	95
	Uric acid in mg/100 ml											
Male												
12 years	643	2,032	4.4	1.12	0.05	2.7	3.0	3.6	4.3	5.1	6.0	6.4
13 years	626	2,006	5.0	1.25	0.05	3.2	3.5	4.2	5.0	5.8	6.6	7.1
14 years	618	1,951	5.5	1.21	0.05	3.6	4.0	4.7	5.5	6.2	7.0	7.7
15 years	613	1,900	5.8	1.24	0.07	4.0	4.4	5.0	5.8	6.7	7.6	8.0
16 years	556	1,836	5.9	1.22	0.09	3.9	4.5	5.2	5.9	6.6	7.5	8.1
17 years	489	1,764	5.9	1.18	0.07	4.2	4.4	5.1	5.8	6.6	7.3	7.8
Female												
12 years	547	1,970	4.6	1.04	0.05	3.0	3.3	3.9	4.5	5.2	6.0	6.5
13 years	582	1,946	4.6	1.12	0.05	2.9	3.2	3.9	4.5	5.2	6.0	6.5
14 years	586	1,901	4.6	1.05	0.05	3.1	3.4	4.0	4.6	5.3	6.0	6.6
15 years	503	1,851	4.7	1.06	0.04	3.2	3.4	4.0	4.6	5.3	6.0	6.5
16 years	536	1,789	4.6	1.09	0.06	3.1	3.4	3.8	4.5	5.2	5.9	6.6
17 years	469	1,746	4.6	1.08	0.05	3.0	3.3	3.9	4.5	5.2	6.0	6.4

NOTE: n — sample size; N — estimated number of children in thousands; X — mean; $s_{\bar{X}}$ — standard deviation; $s_{\bar{X}}$ — standard error of the mean.

Table 4. Estimated number of white youths aged 12-17 years in the population by uric acid groups, sex, and age: United States, 1966-70

Uric acid group	Male						Female					
	12 years	13 years	14 years	15 years	16 years	17 years	12 years	13 years	14 years	15 years	16 years	17 years
	Estimated number of youths in population in thousands											
All groups	1,747	1,729	1,686	1,646	1,594	1,528	1,685	1,667	1,633	1,594	1,542	1,502
Under 1.0 mg percent	—	—	—	—	—	—	—	—	—	—	—	—
1.0-1.4 mg percent	—	—	—	—	4	—	—	—	—	—	—	—
1.5-1.9 mg percent	4	—	—	—	—	—	8	7	—	4	—	—
2.0-2.4 mg percent	34	12	—	—	—	—	18	22	19	14	15	40
2.5-2.9 mg percent	78	24	7	—	17	4	34	54	24	21	28	25
3.0-3.4 mg percent	212	112	32	16	11	18	152	116	119	129	103	119
3.5-3.9 mg percent	332	191	99	43	31	14	191	232	215	184	282	218
4.0-4.4 mg percent	274	257	166	115	57	109	392	365	345	290	265	334
4.5-4.9 mg percent	282	268	239	163	128	187	335	327	307	363	309	243
5.0-5.4 mg percent	201	284	287	275	258	255	238	241	270	246	251	233
5.5-5.9 mg percent	133	213	275	292	298	269	124	125	153	168	122	128
6.0-6.4 mg percent	125	164	235	200	314	248	92	77	79	88	68	89
6.5-6.9 mg percent	38	83	143	181	174	184	67	50	54	36	40	32
7.0-7.4 mg percent	22	59	87	171	134	115	25	29	35	18	31	18
7.5-7.9 mg percent	10	28	60	98	70	57	4	5	7	11	14	8
8.0-8.4 mg percent	3	14	41	49	49	24	4	6	3	7	—	12
8.5-8.9 mg percent	—	10	11	38	35	14	—	4	—	15	5	4
9.0-9.4 mg percent	—	5	3	—	4	17	—	3	—	—	2	—
9.5 mg percent and over	—	5	3	6	11	12	—	6	2	—	4	—

Table 5. Estimated number of Negro youths aged 12-17 years in the population, by uric acid groups, sex, and age: United States, 1966-70

Uric acid group	Male						Female					
	12 years	13 years	14 years	15 years	16 years	17 years	12 years	13 years	14 years	15 years	16 years	17 years
	Estimated number of youths in population in thousands											
All groups	280	262	256	241	231	225	272	275	266	235	243	237
Under 1.0 mg percent	—	—	—	—	—	—	—	—	—	—	—	—
1.0-1.4 mg percent	—	—	—	—	—	—	—	—	—	—	—	—
1.5-1.9 mg percent	2	3	—	—	—	—	—	—	3	3	—	2
2.0-2.4 mg percent	10	—	3	—	—	—	11	8	6	5	7	—
2.5-2.9 mg percent	51	19	17	5	14	—	16	32	18	9	13	14
3.0-3.4 mg percent	36	25	17	12	4	3	25	37	42	39	39	33
3.5-3.9 mg percent	56	29	37	14	22	13	81	47	48	49	74	45
4.0-4.4 mg percent	57	26	27	49	16	43	58	39	61	38	35	42
4.5-4.9 mg percent	32	25	26	52	26	21	48	37	44	40	29	44
5.0-5.4 mg percent	17	52	41	36	37	26	18	46	29	26	19	26
5.5-5.9 mg percent	7	26	35	26	43	35	5	10	8	10	21	6
6.0-6.4 mg percent	7	28	29	25	41	31	3	17	5	13	—	15
6.5-6.9 mg percent	3	19	6	10	9	26	7	—	2	—	3	6
7.0-7.4 mg percent	2	3	10	5	8	10	—	—	—	2	3	—
7.5-7.9 mg percent	—	7	2	3	5	14	—	—	—	—	—	2
8.0-8.4 mg percent	—	—	3	3	3	—	—	—	—	—	—	—
8.5-8.9 mg percent	—	—	3	—	—	—	—	—	—	—	—	—
9.0-9.4 mg percent	—	—	—	—	4	4	—	—	—	—	—	—
9.5 mg percent and over	—	—	—	—	—	—	—	—	—	—	—	—

Table 6. Percent distribution of white youths aged 12-17 years by uric acid groups, according to sex and age: United States, 1966-70

Uric acid group	Male						Female					
	12 years	13 years	14 years	15 years	16 years	17 years	12 years	13 years	14 years	15 years	16 years	17 years
	Percent distribution											
All groups	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Under 1.0 mg percent .	—	—	—	—	—	—	—	—	—	—	—	—
1.0-1.4 mg percent ..	—	—	—	—	0.2	—	—	—	—	—	—	—
1.5-1.9 mg percent ..	0.2	—	—	—	—	—	0.5	0.4	—	0.2	—	—
2.0-2.4 mg percent ..	1.9	0.7	—	—	—	—	1.1	1.3	1.2	0.9	1.0	2.7
2.5-2.9 mg percent ..	4.5	1.4	0.4	—	1.1	0.3	2.0	3.3	1.5	1.3	1.8	1.7
3.0-3.4 mg percent ..	12.1	6.5	1.9	1.0	0.7	1.2	9.0	7.0	7.3	8.1	6.7	7.9
3.5-3.9 mg percent ..	19.0	11.1	5.9	2.6	2.0	0.9	11.4	13.9	13.2	11.6	18.3	14.5
4.0-4.4 mg percent ..	15.7	14.9	9.8	7.0	3.6	7.1	23.3	21.9	21.1	18.2	17.2	22.2
4.5-4.9 mg percent ..	16.1	15.5	14.2	9.9	8.0	12.2	19.9	19.6	18.8	22.7	20.0	16.1
5.0-5.4 mg percent ..	11.5	16.5	17.0	16.7	16.2	16.7	14.1	14.4	16.5	15.4	16.3	15.5
5.5-5.9 mg percent ..	7.6	12.3	16.3	17.7	18.7	17.6	7.4	7.5	9.4	10.6	7.9	8.5
6.0-6.4 mg percent ...	7.2	9.5	13.9	12.1	19.7	16.2	5.5	4.6	4.8	5.5	4.4	5.9
6.5-6.9 mg percent ..	2.2	4.8	8.5	11.0	10.9	12.1	4.0	3.0	3.3	2.3	2.6	2.1
7.0-7.4 mg percent ..	1.3	3.4	5.1	10.4	8.4	7.5	1.5	1.7	2.1	1.1	2.0	1.2
7.5-7.9 mg percent ..	0.6	1.6	3.6	6.0	4.4	3.7	0.2	0.3	0.4	0.7	0.9	0.5
8.0-8.4 mg percent ..	0.2	0.8	2.4	3.0	3.1	1.6	0.2	0.3	0.2	0.5	—	0.8
8.5-8.9 mg percent ..	—	0.6	0.7	2.3	2.2	0.9	—	0.2	—	0.9	0.3	0.2
9.0-9.4 mg percent ..	—	0.3	0.2	—	0.2	1.1	—	0.2	—	—	0.2	—
9.5 mg percent and over	—	0.3	0.2	0.4	0.7	0.8	—	0.4	0.1	—	0.3	—

NOTE: Percents may not add to 100.0 due to rounding.

Table 7. Percent distribution of Negro youths aged 12-17 years by uric acid groups, according to sex and age: United States, 1966-70

Uric acid group	Male						Female					
	12 years	13 years	14 years	15 years	16 years	17 years	12 years	13 years	14 years	15 years	16 years	17 years
	Percent distribution											
All groups	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Under 1.0 mg percent .	—	—	—	—	—	—	—	—	—	—	—	—
1.0-1.4 mg percent ..	—	—	—	—	—	—	—	—	—	—	—	—
1.5-1.9 mg percent ..	0.7	1.2	—	—	—	—	—	—	1.0	1.1	—	0.9
2.0-2.4 mg percent ..	3.4	—	1.2	—	—	—	3.9	3.0	2.2	2.2	2.8	—
2.5-2.9 mg percent ..	18.4	7.2	6.7	2.2	6.2	—	6.1	11.7	6.7	3.8	5.2	6.1
3.0-3.4 mg percent ..	12.9	9.6	6.4	5.1	1.6	1.5	9.2	13.5	15.8	16.4	16.1	14.0
3.5-3.9 mg percent ..	20.0	11.1	14.3	5.6	9.3	5.8	29.8	17.2	17.9	21.0	30.5	19.2
4.0-4.4 mg percent ..	20.2	9.8	10.6	20.5	7.0	19.2	21.4	14.3	23.0	16.2	14.5	17.7
4.5-4.9 mg percent ..	11.4	9.6	10.2	21.7	11.2	9.3	17.8	13.5	16.5	17.2	12.1	18.4
5.0-5.4 mg percent ..	6.1	19.9	16.0	15.0	15.9	11.5	6.5	16.8	11.1	11.3	7.9	11.0
5.5-5.9 mg percent ..	2.6	9.9	13.7	10.8	18.5	15.3	1.8	3.8	2.8	4.3	8.6	2.6
6.0-6.4 mg percent ...	2.6	10.8	11.4	10.2	17.7	13.7	1.1	6.1	2.1	5.5	—	6.5
6.5-6.9 mg percent ..	1.0	7.1	2.5	4.3	4.1	11.7	2.4	—	0.9	—	1.1	2.7
7.0-7.4 mg percent ..	0.6	1.3	3.9	2.0	3.4	4.2	—	—	—	0.9	1.2	—
7.5-7.9 mg percent ..	—	2.5	0.9	1.2	2.0	6.0	—	—	—	—	—	1.0
8.0-8.4 mg percent ..	—	—	1.1	1.3	1.4	—	—	—	—	—	—	—
8.5-8.9 mg percent ..	—	—	1.1	—	—	—	—	—	—	—	—	—
9.0-9.4 mg percent ..	—	—	—	—	1.6	1.6	—	—	—	—	—	—
9.5 mg percent and over	—	—	—	—	—	—	—	—	—	—	—	—

NOTE: Percents may not add to 100.0 due to rounding.

Table 8. Unweighted and weighted sample sizes, mean uric acid, standard deviation, standard error, and selected percentiles, by race, sex, and age: United States, 1966-70

Race, sex, and age	n	N	$\bar{X}$	s_X	$s_{\bar{X}}$	Percentile						
						5	10	25	50	75	90	95
	Uric acid in mg/100 ml											
White male												
12 years	540	1,747	4.5	1.11	0.05	2.9	3.2	3.7	4.4	5.2	6.1	6.4
13 years	542	1,729	5.1	1.24	0.05	3.2	3.6	4.2	5.0	5.8	6.6	7.2
14 years	527	1,686	5.6	1.16	0.05	3.8	4.1	4.8	5.5	6.3	7.1	7.8
15 years	525	1,646	6.0	1.21	0.07	4.1	4.5	5.1	5.9	6.9	7.6	8.1
16 years	496	1,594	6.0	1.19	0.08	4.2	4.6	5.3	6.0	6.6	7.6	8.2
17 years	417	1,528	5.9	1.16	0.08	4.2	4.5	5.1	5.8	6.6	7.3	7.9
White female												
12 years	455	1,685	4.6	1.04	0.06	3.0	3.4	4.0	4.6	5.2	6.1	6.6
13 years	490	1,667	4.6	1.12	0.06	3.0	3.3	4.0	4.6	5.3	6.0	6.6
14 years	484	1,633	4.7	1.05	0.06	3.2	3.5	4.0	4.6	5.4	6.1	6.7
15 years	425	1,594	4.7	1.06	0.05	3.2	3.5	4.1	4.7	5.4	6.1	6.6
16 years	441	1,542	4.7	1.09	0.06	3.2	3.5	3.9	4.6	5.3	6.0	6.6
17 years	393	1,502	4.6	1.08	0.06	3.0	3.4	3.9	4.5	5.2	6.0	6.5
Negro male												
12 years	101	280	3.9	1.02	0.09	2.6	2.7	3.1	3.8	4.5	5.2	5.9
13 years	80	262	4.9	1.32	0.11	2.8	3.2	3.9	5.0	5.7	6.8	7.0
14 years	88	256	4.9	1.32	0.19	2.8	3.3	3.8	5.1	5.8	6.4	7.0
15 years	84	241	5.0	1.09	0.12	3.4	3.8	4.3	4.7	5.7	6.4	7.0
16 years	57	231	5.3	1.28	0.24	2.9	3.7	4.5	5.5	6.1	6.9	7.5
17 years	69	225	5.6	1.27	0.22	3.8	4.1	4.4	5.6	6.5	7.1	7.6
Negro female												
12 years	88	272	4.1	0.89	0.11	2.6	3.1	3.6	4.0	4.6	5.1	5.6
13 years	91	275	4.2	1.05	0.10	2.6	2.8	3.4	4.1	5.0	5.5	6.1
14 years	101	266	4.1	0.92	0.12	2.6	2.9	3.5	4.2	4.7	5.3	5.8
15 years	73	235	4.2	0.99	0.13	2.9	3.2	3.6	4.1	5.0	5.6	6.1
16 years	93	243	4.1	0.93	0.12	2.8	3.1	3.5	4.0	4.7	5.5	5.8
17 years	74	237	4.3	1.03	0.17	2.9	3.2	3.6	4.2	4.9	6.1	6.2

NOTE: n — sample size; N — estimated number of children in thousands; $\bar{X}$ — mean; $s_{\bar{X}}$ — standard deviation; s_X — standard error of the mean.

Table 9. Percentage of white and Negro youths aged 12-17 years with uric acid levels above 7.9, 8.4, and 8.9 mg/100 ml: United States, 1966-70

Sex and uric acid levels	Age in years											
	12	13	14	15	16	17	12	13	14	15	16	17
Male	Percent white						Percent Negro					
Above 7.9 mg/100 ml	0.2	2.0	3.5	5.7	6.2	4.4	—	—	2.2	1.3	3.0	1.6
Above 8.4 mg/100 ml	—	1.2	1.1	2.7	3.1	2.8	—	—	1.1	—	1.6	1.6
Above 8.9 mg/100 ml	—	0.6	0.4	0.4	0.9	1.9	—	—	—	—	1.6	1.6
Female												
Above 7.9 mg/100 ml	0.2	1.1	0.3	1.4	0.8	1.0	—	—	—	—	—	—
Above 8.4 mg/100 ml	—	0.8	0.1	0.9	0.8	0.2	—	—	—	—	—	—
Above 8.9 mg/100 ml	—	0.6	0.1	—	0.5	—	—	—	—	—	—	—

Table 10. Weighted sample size, mean uric acid, and standard error of the mean for youths, by age, sex, and annual family income: United States, 1966-70

Sex and annual family income	12 years			13 years			14 years			15 years			16 years			17 years		
	N	$\bar{X}$	$s_{\bar{X}}$	N	$\bar{X}$	$s_{\bar{X}}$	N	$\bar{X}$	$s_{\bar{X}}$	N	$\bar{X}$	$s_{\bar{X}}$	N	$\bar{X}$	$s_{\bar{X}}$	N	$\bar{X}$	$s_{\bar{X}}$
Male	Uric acid in mg/100 ml																	
All incomes	2,032	4.4	0.05	2,006	5.0	0.05	1,951	5.5	0.05	1,900	5.8	0.07	1,836	5.9	0.09	1,764	5.8	0.07
Less than $3,000	180	4.0	0.17	212	4.8	0.22	200	5.4	0.16	241	5.5	0.16	201	6.1	0.18	226	5.8	0.11
$3,000-$4,999	308	4.4	0.12	264	5.0	0.17	240	5.5	0.17	219	6.0	0.17	265	5.9	0.14	245	6.0	0.14
$5,000-$9,999	869	4.4	0.08	767	5.1	0.09	746	5.4	0.09	719	5.9	0.11	719	5.8	0.13	692	5.8	0.08
$10,000 or more	575	4.4	0.07	619	5.1	0.11	597	5.5	0.08	598	5.9	0.10	516	5.9	0.13	479	6.0	0.12
Don't know	55	4.5	0.26	65	5.6	0.28	100	5.7	0.34	76	6.1	0.27	82	5.9	0.26	49	5.3	0.52
Blank or refused	46	3.9	0.28	80	4.6	0.27	67	6.0	0.22	46	6.3	0.34	55	6.3	0.23	74	5.4	0.25
Female																		
All incomes	1,970	4.6	0.05	1,946	4.6	0.05	1,901	4.6	0.05	1,851	4.7	0.04	1,789	4.6	0.06	1,746	4.6	0.05
Less than $3,000	257	4.6	0.15	268	4.3	0.17	213	4.4	0.21	258	4.5	0.17	246	4.6	0.13	182	4.4	0.18
$3,000-$4,999	274	4.5	0.20	301	4.7	0.14	300	4.5	0.10	264	4.5	0.12	166	4.2	0.13	206	4.5	0.17
$5,000-$9,999	722	4.6	0.08	802	4.6	0.09	720	4.6	0.09	700	4.7	0.07	650	4.6	0.09	586	4.6	0.09
$10,000 or more	600	4.5	0.10	494	4.6	0.09	554	4.8	0.09	533	4.9	0.08	594	4.6	0.09	628	4.6	0.08
Don't know	79	4.4	0.23	46	4.5	0.25	72	4.5	0.23	63	4.5	0.17	83	4.8	0.14	92	4.6	0.15
Blank or refused	37	4.5	1.12	35	4.6	0.37	42	4.5	0.31	32	4.9	0.61	50	5.1	0.33	52	4.8	0.55

NOTE: N – estimated number of children in thousands; $\bar{X}$ – mean; $s_{\bar{X}}$ – standard error of the mean.

Table 11. Weighted sample size, mean uric acid, and standard error of the mean for youths, by age, sex, and education of parent: United States, 1966-70

Sex and education of parent	12 years			13 years			14 years			15 years			16 years			17 years		
	N	$\bar{X}$	$s_{\bar{X}}$	N	$\bar{X}$	$s_{\bar{X}}$	N	$\bar{X}$	$s_{\bar{X}}$	N	$\bar{X}$	$s_{\bar{X}}$	N	$\bar{X}$	$s_{\bar{X}}$	N	$\bar{X}$	$s_{\bar{X}}$
Male	Uric acid in mg/100 ml																	
All education groups .	2,032	4.4	0.05	2,006	5.0	0.05	1,951	5.5	0.05	1,900	5.8	0.07	1,836	5.9	0.09	1,764	5.8	0.07
Less than 8 years	176	4.2	0.25	175	5.1	0.23	172	5.7	0.22	196	5.7	0.17	217	5.9	0.30	208	5.6	0.32
8-11 years	543	4.2	0.07	502	5.1	0.10	474	5.3	0.13	487	5.8	0.11	474	5.9	0.14	446	5.8	0.10
12 years	736	4.5	0.09	780	5.0	0.08	730	5.4	0.08	727	5.8	0.10	630	5.9	0.09	668	5.9	0.10
13 years or more	562	4.5	0.09	527	5.0	0.10	549	5.6	0.09	472	6.0	0.12	480	6.0	0.14	388	6.0	0.09
Unknown	16	*	*	23	5.3	0.33	25	4.9	0.87	18	6.3	0.54	35	6.0	0.33	54	5.9	0.65
Female																		
All education groups .	1,970	4.6	0.05	1,946	4.6	0.05	1,901	4.6	0.05	1,851	4.7	0.04	1,789	4.6	0.06	1,746	4.6	0.05
Less than 8 years	211	4.7	0.16	228	4.6	0.19	160	4.4	0.24	178	4.7	0.20	167	4.5	0.18	146	4.5	0.22
8-11 years	480	4.5	0.07	507	4.4	0.10	537	4.4	0.08	598	4.5	0.09	453	4.4	0.09	465	4.7	0.07
12 years	729	4.6	0.10	727	4.8	0.07	719	4.7	0.08	640	4.7	0.08	623	4.8	0.08	525	4.6	0.11
13 years or more	509	4.5	0.09	463	4.5	0.11	465	4.8	0.10	411	4.9	0.05	512	4.7	0.11	542	4.5	0.09
Unknown	41	4.2	0.26	22	*	*	21	4.3	0.44	22	*	*	34	4.5	0.37	67	4.5	0.34

NOTE: N – estimated number of children in thousands; $\bar{X}$ – mean; $s_{\bar{X}}$ – standard error of the mean.

Table 12. Weighted sample size, mean uric acid, and standard error of the mean for Negro and white female youths aged 12-17 years, by annual family income and education of parent: United States, 1966-70

Variable	Negro female			White female		
	N	$\bar{X}$	$s_{\bar{X}}$	N	$\bar{X}$	$s_{\bar{X}}$
Annual family income	Uric acid in mg/100 ml					
Less than $3,000	495	4.2	0.09	928	4.6	0.11
$3,000-4,999	400	4.1	0.07	1102	4.7	0.10
$5,000-9,999	407	4.2	0.10	3760	4.7	0.05
$10,000 and over	117	4.0	0.21	3258	4.7	0.05
Education of parent						
Less than 8 years	302	4.1	0.10	784	4.7	0.14
8-11 years	679	4.1	0.12	2337	4.6	0.04
12 years	363	4.3	0.09	3600	4.7	0.06
13 years or more	127	4.3	0.15	2752	4.6	0.05

NOTE: N – estimated number of children in thousands; $\bar{X}$ – mean; $s_{\bar{X}}$ – standard error of the mean.

Table 13. Mean uric acid, standard error of the mean, and weighted sample size for white youths, by place of residence, sex, and age: United States, 1966-70

Sex and age	Place of residence								
	Central city of SMSA[1]			Suburban areas			Rural farm area		
	$\bar{X}$	$s_{\bar{X}}$	N	$\bar{X}$	$s_{\bar{X}}$	N	$\bar{X}$	$s_{\bar{X}}$	N
	Uric acid in mg/100 ml								
Male									
12 years	4.4	0.11	363	4.4	0.11	700	4.8	0.22	110
13 years	5.2	0.11	400	5.1	0.10	615	5.3	0.17	123
14 years	5.6	0.12	369	5.5	0.09	594	5.8	0.27	125
15 years	6.0	0.18	376	6.0	0.14	579	6.1	0.21	137
16 years	6.0	0.16	338	6.0	0.12	550	6.3	0.26	153
17 years	6.0	0.22	372	5.9	0.12	441	6.2	0.14	119
Female									
12 years	4.7	0.09	356	4.6	0.11	649	5.0	0.36	127
13 years	4.7	0.13	407	4.7	0.11	522	4.8	0.15	132
14 years	4.6	0.14	339	4.8	0.12	572	5.0	0.35	119
15 years	4.8	0.14	335	4.9	0.10	580	4.5	0.11	134
16 years	4.6	0.14	360	4.7	0.07	591	4.7	0.20	67
17 years	4.7	0.13	392	4.5	0.11	531	4.7	0.18	121

[1] Standard Metropolitan Statistical Area.

NOTE: $\bar{X}$ — mean; $s_{\bar{X}}$ — standard error of the mean; N — estimated number of youths in thousands.

Table 14. Mean uric acid levels found in Tecumseh, Mich., compared with HES findings reduced by 0.5 mg/100 ml

Age group	Male		Female	
	Tecumseh mean	HES adjusted mean	Tecumseh mean	HES adjusted mean
12 years	4.2	3.9	4.2	4.1
13 years	4.6	4.5	4.3	4.1
14 years	5.0	5.0	4.5	4.1
15 years	5.5	5.3	4.1	4.2
16 years	5.5	5.4	4.4	4.1
17 years	5.7	5.4	4.1	4.1

NOTE: The first Tecumseh study, conducted in 1959-60, yielded the only data on uric acid level detailed enough to compare age for age and for sex with HES findings. Because the Tecumseh data were determined by enzymatic (uricase) assay, and those of HES by a colorimetric method, mathematical adjustment was necessary so as to enable comparison.

APPENDIX I

TECHNICAL NOTES ON METHODS

The Survey Design

The sampling plan of Cycle III of the Health Examination Survey followed a multistage, stratified probability sample of clusters of households in land-based segments in which a sample of the U.S. population (including Alaska and Hawaii) aged 12 through 17 years was selected. Excluded were those youths confined to institutions and those residing on any of the reservation lands set aside for use by American Indians.

The sample design of Cycle III is similar to that of Cycle II in that it uses the same 40 sample areas and the same segments. The decision to incorporate this feature into Cycle III was not made prior to the selection of the Cycle II sample, although it is consistent with the initial concept of a single program for persons 6-17 years old. The final decision to use this identical sampling frame was made during the operation of the Cycle II program.

The successive elements for this sample design are primary sampling unit; census enumeration district; segment (a cluster of households); household; all eligible youths; and finally, the sample youth. Every eligible youth within the defined population has a known and approximately equal chance for selection into the sample.

The steps of drawing the sample were carried out jointly with the U.S. Bureau of the Census; the starting points were the 1960 decennial census lists of addresses and the nearly 1,900 primary sampling units (PSU's) into which the entire United States was divided. Each PSU is a standard metropolitan statistical area (SMSA), a county, or a group of two or three contiguous counties. These PSU's were grouped into 40 strata so that each stratum had an average size of about 4.5 million persons. This grouping maximized the degree of homogeneity of the PSU's within each strata with regard to the population size, degree of urbanization, geographic proximity to one another, and degree of industrialization. The 40 strata were then classified into four broad geographic regions of 10 strata each and, within each region, cross-classified by four population density classes and by the rates of population change from 1950 to 1960. Using a modified Goodman-Kish controlled-selection technique, one PSU was drawn from each of the 40 strata.

The sampling within the PSU's was carried out in several steps. The first step was the selection of census enumeration districts (ED's)—small, well-defined areas of about 250 housing units. The entire nation was divided into ED's for the 1960 population census, and each ED was assigned a "measure of size" equal to the rounded whole number resulting from a "division by nine" of the number of children aged 5-9 in the ED at the time of the 1960 census. A sample of 20 ED's in the sample PSU was selected according to a systematic sampling technique, with each ED having a probability of selection proportional to the population of children aged 5-9 years at the time of the 1960 census date. From each ED a random selection of one measure of size (segment) was taken.

Minor changes required in the Cycle III design were (1) that it be supplemented for new construction to a greater extent than had been necessary in Cycle II and (2) that reserve segments be added. Although it was the plan for Cycle III to use the Cycle II segments, it was recognized that within several PSU's additional reserve segments would be needed to avoid the risk of having an insufficient number of examinees. This was prompted by the fact that four of the PSU's in Cycle II had yields of less than 165 eligible children and several others were marginal in their yield. In addition, there was a 3-year interval between Cycle II and Cycle III, so that it was quite possible for some segments to have been completely demolished due to highway construction or urban redevelopment.

The time available for examinations at a particular location, or stand, is necessarily set far in advance of any preliminary field work at the stand. Therefore, the number of examinations that can be performed at a particular location is dependent on the number of examining days available. At the majority of locations, the number of days available, excluding Saturdays, is 17. At the rate of 12 examinations each day, this provides for 204 examination slots. Examinations are conducted on Saturdays if necessary. Because of rescheduling for cancellations or no-shows, the maximum number of youths that is considered for inclusion in the sample is 200. When the number of eligible youths exceeds the maximum, subsampling is performed to reduce the number to manageable limits. This is accomplished through the use of a master list, which is a listing of all eligible youths in order by segment, serial number (household order within segment), and column number (order in the household by age). After the subsampling rate has been determined, every nth name on the list is deleted, starting with the yth name, y being a randomly selected number between 1 and n. Youths who are deleted from the Cycle III sample but who were examined in Cycle II and any twin who may have been deleted are scheduled, if time permits, for an examination to be included only in the longitudinal study portion or twin study portion of the survey. Their data are not included in the report as part of the regular sample.

Since the strata are roughly equal in population size and a nearly equal number of sample youths were examined in each of the sample PSU's, the sample design is essentially self-weighting with respect to the target population; that is, each youth 12 through 17 years old had about the same probability of being drawn into the sample.

The adjustment upward for nonresponse is intended to minimize the impact of nonresponse on final estimates by imputing to nonrespondents the characteristics of "similar" respondents. Here "similar" respondents were judged to be examined youths in a sample PSU having the same age (in years) and sex as those not examined in that sample PSU.

The poststratified ratio adjustment used in Cycle III achieved most of the gains in precision that would have been attained if the sample had been drawn from a population stratified by age, color, and sex, and it made the final sample estimates of population agree exactly with independent controls prepared by the U.S. Bureau of the Census for the noninstitutional population of the United States as of March 9, 1968 (approximate midsurvey point) by color and sex for each single year of age 12 through 17. The sampling weight of every youth examined in each of the 24 age, race, and sex classes is adjusted upward or downward so that the weighted total within the class equals the independent population control.

A more detailed description of the sampling plan and estimation procedures is included in *Vital and Health Statistics*, Series 2-Number 43,[44] and in Series 1-Numbers 1[1], 5[3], and 8[4], which describe the plan and operation of the first three cycles of the Health Examination Survey.

Some Notes on Response Rates

As mentioned previously, the sample designs of the second and third cycles of the HES were

Note.—A list of references follows the text.

similar. Differences did occur, however, in response rates of various subgroups of these samples, and these differences deserve some consideration here.

Most importantly, the number of youths selected for examination increased from 7,417 in Cycle II to 7,514 in Cycle III. The response rate—i.e., the number of youths selected who were actually examined—decreased from 96 percent in Cycle II to 90 percent in Cycle III. Of the youths examined in Cycle II, 13.9 percent were Negro, compared with 14.8 percent of those examined in Cycle III. This difference does not reflect a difference in the percentage of Negro youths selected for examination, but rather, a smaller decrease in response rate for Negro youths between the two cycles than was the case for white youths. In actuality, 13.8 percent of the sample selected for examination was Negro in Cycle III, corresponding to 13.5 percent in Cycle II. However, whereas the response rate for white youths dropped from 95.6 percent in Cycle II to 89.1 percent in Cycle III, the response rate for Negro youths dropped far less, from 98.4 percent to 96.6 percent. Thus, relatively better response from the Negro portion of the sample in Cycle III increased their percentage of actual examinations as compared with the previous cycle.

Examination of sample sizes in this report clearly shows that at every age group, fewer females than males were actually examined. This, again, is not attributed to differences in numbers of youths selected in the sampling design, but rather to the following differential response rates between males and females:

Age	Male	Female
Total	91.4	88.7
12	93.5	91.3
13	93.2	91.9
14	91.7	90.7
15	91.6	87.9
16	89.8	87.7
17	87.6	81.8

Note that at each age group the response rate for males exceeded that for females.

A similar analysis of response rates can be done by age, race, and sex, as follows:

Age	White male	Negro male	White female	Negro female
Total	90.5	97.6	87.4	95.8
12	92.6	99.0	90.1	98.9
13	92.5	98.8	91.1	96.8
14	91.0	97.8	89.6	96.2
15	90.7	97.7	86.4	98.6
16	89.2	95.0	86.6	93.0
17	86.5	95.8	80.2	91.4

The above clearly indicates that for all ages under consideration in Cycle III of the HES, the response rate for Negro youths exceeded that for white youths of the same sex and age.

Reasons for differences in response rates are many, but may range from the incentive to get examined in order to miss a day of school, to fear of the examination itself, to inhibitions with respect to being examined. The worst response rate was recorded for the oldest females, that is, those aged 17 years.

Parameter and Variance Estimates

Because each of the 6,768 sample children has an assigned statistical weight, all estimates of population parameters presented in HES publications are computed taking this weight into consideration. Thus, $\bar{X}$, the estimate of a population mean μ is computed as follows:

$$\bar{X} = \frac{\sum_{i=1}^{n} W_i X_i}{\sum W_i}$$

where X_i is the observation or measurement taken on the ith person and W_i is the statistical weight assigned to that person.

The HES has an extremely complex sampling plan, and obviously, by the very nature of the sample, the estimation procedure is complex as well. For estimating the reliability of findings, a method is required that "reflects both the losses

from clustering sample cases at two stages and the gains from stratification, ratio estimation, and poststratification."[45]

The method for estimating variances in the HES is the half-sample replication technique. The method was developed at the U.S. Bureau of the Census prior to 1957 and has at times been given limited use in the estimation of the reliability of results from the Current Population Survey. This half-sample replication technique is particularly well suited to the HES because the sample, although complex in design, is relatively small (6,768 cases) and is based on but 40 strata. This feature permitted the development of a variance estimation computer program that produces tables containing desired estimates of aggregates, means, or distributions, together with a table identical in format but containing the estimated variance of the estimated statistics. The computations required by the method are simple, and the internal storage requirements are well within the limitation of the IBM 360-50 computer system used at the National Center for Health Statistics.

Variance estimates computed for this report were based on 20 balanced half-sample replications. A half sample was formed by choosing one sample PSU from each of 20 pairs of sample PSU's. The composition of the 20 half samples was determined by an orthogonal plan. To compute the variance of any statistic, that statistic is computed for each of the 20 half samples. Using the mean, $\bar{X}_i$, as an example, the weighted mean of the entire undivided sample ($\bar{\bar{X}}$) is computed. The variance of the mean is the mean square deviation of each of the 20 half-sample means about the overall mean. Symbolically,

$$\mathrm{Var}(\bar{X}) = \frac{\sum_{i=1}^{20} (\bar{X}_i - \bar{\bar{X}})^2}{20}$$

and the standard error of the mean is the square root of $\mathrm{Var}(\bar{X})$. In a similar manner the standard error of any statistic may be computed.

A detailed description of this replication process has been published in *Vital and Health Statistics,* Series 2-Number 14.[45]

Standards of Reliability and Precision

All means, variances, and percentages appearing in this report met defined standards before they were considered acceptably precise and reliable.

The rule for reporting means and percentiles consisted of two basic consecutive criteria: that a sample size be at least five; and that the estimated coefficient of variation (i.e., the standard error of the mean divided by the mean, or $(S_{\bar{X}}/\bar{X})$ be less than 25 percent. Thus, if the sample size was too small, or if, given adequate sample size, the variation with respect to the mean was too large, then the estimate was considered neither precise nor reliable enough to meet the standards established for publication.

Imputation

In addition to the subject nonresponse discussed above, the problem of item nonresponse merits consideration here. In this situation, information about a respondent is complete with the exception of a missing uric acid value.

Missing data were replaced by the value recorded for a randomly selected respondent of similar age, sex, and race. However, when only one of the two uric acid values was missing, the recorded measurement was substituted for the unknown value. This occurred in 38 cases (0.6 percent of total respondents). Imputation where there was no value recorded for examinees was necessary in 199 cases (2.9 percent of total respondents).

In effect, sample cases were sorted into categories, and within each category the cases were expected to have high intraclass correlation (i.e., to be relatively homogeneous). Those with missing values were then completed with a value randomly selected from within the category. This method of imputation preserves both the expected values and the distribution of values in each category of the respondent cases.

APPENDIX II

DEMOGRAPHIC VARIABLES

Regional and demographic characteristics by which the population has been classified for this report are defined as follows:

Age and sex.—Population was classified into 12 age-sex groups—the six ages 12-17 years by sex. Birth certificates verified the age of 92 percent of the youths. Age stated by the parents was accepted as the true age for the other 8 percent. Age is expressed as years attained at last birthday.

Race.—Serum uric acid value was reported by race for white and Negro youths. Youths of other races were not sampled sufficiently for comparison purposes and represented only 0.55 percent of the sample.

Region.—Regional data are presented for four regions of the continental United States.

Region	*States Included*
Northeast . . .	Maine, Vermont, New Hampshire, Massachusetts, Rhode Island, Connecticut, New York, Pennsylvania, New Jersey
Midwest . . .	Minnesota, Wisconsin, Michigan, Iowa, Missouri, Illinois, Indiana, Ohio
South	Delaware, Maryland, Virginia, District of Columbia, West Virginia, Kentucky, Tennessee, North Carolina, South Carolina, Georgia, Florida, Alabama, Mississippi, Arkansas, Louisiana
West	Washington, Oregon, Idaho, Montana, North Dakota, South Dakota, Wyoming, Nebraska, Kansas, Colorado, Utah, Nevada, California, Arizona, New Mexico, Texas, Oklahoma, Alaska, Hawaii

Family Income.—The income recorded was the total income received during the past 12 months by the head of the household and all other household members related to the head by blood, marriage, or adoption. This income was the gross cash income (excluding pay in kind) except in the case of a family with its own farm or business, in which case net income was recorded.

Education of parent or guardian.—This item was recorded as the highest grade that had been completed in school. The only grades counted were those that had been completed in a regular school in which persons were given formal education: graded or private schools, either day or night schools, with either full-time or part-time attendance. A "regular" school is one that advances a person toward an elementary or high school diploma, or a college, university, or professional school degree. Education in vocational, trade, or business schools outside the regular school system was not counted in determining the highest grade of school completed.

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APPENDIX III

TECHNIQUES OF MEASUREMENT AND QUALITY CONTROL

MEASUREMENT

The HES Blood-Drawing Technique and Its Historical Development

For a variety of reasons, it was decided not to attempt to draw blood specimens from children 6-11 years of age in Cycle II. The children included in the national probability sample came from all regions of the country and all cultural and socioeconomic groupings and ways of life. It was assumed, therefore, that some had never been to a physician before and that others would have very bad memories of and associations with such visits. In addition, because the sample covered the entire spectrum of behavioral and physical development extant in the United States, severe technical and behavioral problems resulting from immaturity of 6- and 7-year-olds would be likely. It was believed that fear or extreme distaste for having a blood sample drawn on the part of many potential subjects might severely affect the response rate, which is so crucial to a survey like this. When it is remembered that the overall response rate for Cycle II was a remarkable 96 percent, it is difficult to argue with this line of reasoning. Now, of course, it can never be known how great a diminution of the response rate would have been caused by the inclusion of a blood sample from younger children in Cycle II.

In the early planning stages of Cycle III, it was decided to obtain a blood specimen from the youths 12-17 years if at all feasible, that is, primarily if the price in terms of diminished response rate and cooperation of the examinees would not be too high. Accordingly, in three separate pretests, investigations were conducted regarding the problem of developing a satisfactory blood-collection technique for this age group and examination setting. What was desired was to draw the optimum amount of blood, without causing emotional upset to the examinee, or without affecting his performance in any of the procedures to follow. The amount of usable blood that could be drawn posed a limiting factor on the number of blood chemistry tests that could be performed and greatly influenced the acceptance or rejection of an entire possible area of the examination, such as the nutritional assessment. Logistical problems also had to be resolved involving the handling, separating, and packaging of drawn blood so that there would be a minimum of blood loss and packaging error. For the refrigerated but unfrozen blood, time from shipment to delivery was critical; therefore, arrangements had to be made with postal authorities to assure prompt delivery to the laboratories in order to avoid spoilage.

There was a trial-and-error process, and there was good advice and help from many sources in developing a satisfactory blood-drawing technique. The chief sources of help, outside of the immediate HES technical staff, were Dr. Wilma Bias and Dr. Bernice Cohen of The Johns Hopkins University; Dr. Gerald Cooper, Chief of Laboratories, Communicable Disease Center, Public Health Service, Atlanta, Ga.; the many teenage subjects during our pretest who gave valuable suggestions and who pointed out, either

as overt advice or by their immediate reactions, specific points to be avoided; and, finally, the professional and technical division of the Becton-Dickinson Company, Rutherford, N.J. The latter, through several personal visits by a representative of their technical division, not only gave excellent technical advice on blood-collection techniques and the use of alternative equipment, but also devised a special fitting that made the transfer from one vacutainer tube to another much smoother.

During the pretesting, it was learned that many subjects did not like to see any part of the blood-drawing procedure, including their own blood in tubes. Therefore, a technique was employed that minimized the subject's attention to the operation. Effective screening was achieved by having the subject lie down and by draping and keeping the arm and tubes well below the level of the examination table. After the skin area was cleansed with alcohol, the blood was drawn from the antecubital fossa by the physician-nurse team. At the discretion of the physician, a tourniquet was used to fill the vein; however, once the needle was inserted into the vein, the tourniquet was taken off the arm so that the blood flowed freely.

A B-D blood culture needle and tube were used to draw blood. Using the specially prepared link fitting, the nurse inserted the short needle into a vacutainer tube holder. The tube was clamped with a hemostat until the vein was punctured and the vacutainer was inserted into the holder.

From the one free-flowing venipuncture, a total of only 55 cm^3 of blood was collected in four separate vacutainer tubes from all male and almost half of the female subjects. (The difference was that all males had separate plasma drawn to be frozen and stored for future testosterone determination and almost half of the females provided a replicate blood specimen for quality control of the laboratory determinations; the remaining females had 40 cm^3 drawn.)

Each test tube was labeled with the examinee's number and left in the test-tube holding rack at room temperature for 1 hour. The nurse then placed the tubes in the laboratory refrigerator, along with 10 extra examinee identification labels for use by the technicians.

An analysis that attempts to estimate the impact of the addition of a blood sample on the Cycle III sample response rate is in progress.

Serum Uric Acid Determinations

As already described elsewhere in the report, the frozen serum was sent via air freight in styrofoam containers to the Clinical Chemistry Division, CDC, Atlanta, Ga., for the laboratory determinations. The serum uric acid levels were determined by a colorimetric phosphotungstic acid procedure on the Technicon Auto-Analyzer-I using the N-13b method.[e] A description of the general principles of the method and a listing of the equipment used are quoted below. The detailed preparation of the reagents used (which are so crucial to the exact values obtained), a flow diagram of the AutoAnalyzer-I, and the step-by-step procedures are also documented in the report.[e]

Principle: Serum is passed through a dialyzer where uric acid and other dialyzable solutes are separated from protein. The protein-free dialysate is mixed with urea and sodium cyanide reagent, which provides alkalinity, followed by phosphotungstic acid. The phosphotungstic acid is reduced by the uric acid under these conditions to produce a blue-colored substance. The blue color is measured photometrically and read at 660 mμ.[e]

Equipment: The uric acid AutoAnalyzer-I is comprised of the following modules: sampler with 2:1, 40 per hour cam, pump, dialyzer, colorimeter, and recorder. All waste was drained directly into a sink trap and continually flushed with running water so that at no point would it come in contact with acid with which it could combine to form the very poisonous HCN.[e]

MONITORING SYSTEMS

In addition to the sampling considerations already discussed, the quality of data collected is also a special concern. One of the main purposes of the monitoring system employed in the survey was to indicate whether the measurements produced by our measurement process

[e]Procedure N-13b, Technicon Laboratory Method File, 1965, Technicon Instruments Corp., Tarrytown, N.Y.

attained the desired quality. A second major purpose was to make possible quantitative summary descriptions of residual measurement errors to aid in the interpretation of survey data.

The monitoring system as applied to the taking of blood samples consisted of a formal system of replicate examinations (described later in this appendix). Replicate measurements are useful for a variety of reasons; for example, as a means of increasing precision of estimates of individual measurements, as a training technique, and as a monitoring system which includes the objective of overall evaluation of measurement errors. These objectives are not incompatible, and replicate data collected primarily for one of these objectives often indirectly, if not directly, accomplish one or both of the remaining two. For this reason replicate data are most often collected with a combination of these objectives in mind.

Methods of Taking Replicate Measurements

A major source of uncertainty in estimates derived from replicate measurements is in the inability to make the replicate measurement under precisely the same conditions and in the same manner as the original measurement. This uncertainty is difficult to evaluate, and most attempts are restricted to subjective statements concerning the direction and/or size of the bias and the need for concern in the analysis of data.

In this study two extra blood samples were drawn from a subsample of Cycle III examinees and were included in the shipment sent for processing to the Lipid Standardization Laboratory (now called the Clinical Chemistry and Hematology Laboratory) at the Communicable Disease Center in Atlanta, Ga. Replicate blood samples were taken from the same venipuncture as the regular blood samples and, from shipment to final processing at the Communicable Disease Center, were treated the same as the regular samples. These replicates were labeled with dummy examination identification numbers and were recorded by the nurse in a replicate log book. All samples were submitted for laboratory analysis with no indication that any two samples came from the same examinee. Each sample was split by the technician and duplicate determinations were performed; if a difference greater than 0.4 mg/100 ml was found (it was usually a reading or recording error), a third determination was performed and the two closest determinations were used. The analyses of replicates and originals were performed under identical laboratory conditions by the same technician in a true double-blind manner.

Cycle III examinees were chosen systematically for replicate blood determinations. On every third day of the first 15 days of each Examination Center, two extra blood samples were drawn (preferably from girls) for the replicate study. Since in a voluntary survey it is impossible to follow a statistically random process in scheduling subjects, the replicate design did not ensure that its subjects would be "representative" of those in the larger Cycle III Health Examination Survey. It is felt, however, that this is not a crucial issue since the matter of concern in undertaking the replicate study is not the determination of possible differences in the values of the measurements, but rather the determination of possible differences in errors associated with the measurements.

Results of the Replicate Study for Uric Acid

Two readings were made of the original split sample obtained for each of the 6,531 (96 percent of the total sample) examinees by the same technician. An extra blood sample was drawn for replicate studies on 424 examinees of which 96 percent were adequate.

Frequency and percent distributions of the absolute differences between the duplicated determinations on the original uric acid specimen and also between the duplicated determinations on the replicate and original uric acid specimens are presented in table I. The first two columns represent the differences between the duplicated determinations on the original specimen; the second two columns represent the differences between the first recorded determination values of the original specimen and that of the replicate specimen; and the third two columns represent

Table I. Frequency and percent distribution of absolute differences between duplicated determinations of original specimens and between original and replicated specimens

Absolute difference (mg/100 ml)	Difference between duplicated determinations of original specimen		Difference between original and replicated specimens			
			First determinations		Second determinations	
	Frequency	Percent of total	Frequency	Percent of total	Frequency	Percent of total
Total	6,531	100.0	403	100.0	402	100.0
0.0	3,225	49.4	176	43.7	162	40.3
0.1	2,579	39.5	147	36.5	138	34.3
0.2	569	8.7	35	8.7	61	15.2
0.3	114	1.7	19	4.7	13	3.2
0.4	25	0.4	7	1.7	8	2.0
0.5	6	0.1	3	0.7	3	0.7
0.6	5	0.1	1	0.2	1	0.2
0.7	1	–	1	0.2	3	0.7
0.8	1	–	1	0.2	–	–
0.9	1	–	–	–	1	0.2
1.0	–	–	2	0.5	2	0.5
1.1	1	–	–	–	–	–
1.2	–	–	1	0.2	–	–
1.3	1	–	–	–	–	–
1.4	–	–	1	0.2	1	0.2
1.6	–	–	1	0.2	2	0.5
1.7	–	–	–	–	2	0.5
1.8	–	–	3	0.7	1	0.2
1.9	–	–	2	0.5	1	0.2
2.0	1	–	–	–	–	–
2.3	–	–	1	0.2	2	0.5
2.4	–	–	1	0.2	–	–
3.2	1	–	–	–	–	–
3.3	–	–	1	0.2	1	0.2
5.0	1	–	–	–	–	–

differences between the second (or duplicated) recorded values of the original and replicate specimens.

As a summary statistic of the distribution of differences between replicate and original uric acid determinations shown in table I, we have computed V, the percentage technical error of measurement which is given by

$$V = \frac{100}{\bar{X}} \sqrt{\frac{\sum_{i=1}^{n} d_i^2}{2n}}$$

where

n is the number of pairs of measurements in the study,

d_i^2 is the square of the difference between members of the ith pair of measurements ($i = 1, \ldots, n$), and

$\bar{X}$ is the arithmetic mean of the $2n$ measurements in the study.

The percentage technical error, V, can be interpreted as a "coefficient of variation" and is a dimensionless constant. It essentially describes the size of measurement error relative to the mean value of a measurement. As one measure of the differences between specified determinations the values of V are given below.

Specified Determinations	V
First determinations on original and replicate specimens	5.2 percent
Second determinations on original and replicate specimens	5.1 percent
Duplicated determinations on original specimen	1.8 percent

These values of V, however, mask the essentially excellent reproducibility that technicians at the Communicable Disease Center achieved. When the frequency and percent distributions in table I are examined, more than 95 percent of each of the three distributions in the table are found to be below 0.5 mg/100 ml. The few extreme outliers account for the differences in V noted above.

Data Handling Verification

Quality control considerations were not confined to the laboratory. Data were subject to the possibility of error every time a human hand touched a keyboard or moved a pencil across a page. After the data had been put on punchcards, they were transferred to magnetic tape. Subsequent handling of the data by programmers and transcription by clerks provided other sources of error.

To verify all operations, the entire cohort of 16-year-old Negro males was subjected to a thorough independent manual audit. The computer tape printout of each subject's serum uric acid value was listed opposite his identification. These were individually checked against the values originally recorded at the Communicable Disease Center. The mean was then computed manually on the desk calculator and proved identical to the computer's mean value.

In addition, all age, race, and sex identification for members of this cohort were found to correspond exactly to the information given on the household interview forms completed by census interviewers.

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