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all organs. In his careful review, he stated that most of the data indicate that with inanition there is a marked decrease in the weight of the liver of both man and animals, which tends to be relatively greater than the loss in total body weight. In extreme emaciation the spleen is greatly reduced in weight, the relative loss being twice as great as that of the total body weight, but in early stages of inanition the reduction is slight and difficult to establish because of the great normal variability of the weight of the spleen.

Practically, in the general run of necropsies on adults, the pathologists would probably recognize the reduction in the size of the organ due to old age and hence exclude senile organs from their estimates of normal weight, but they would constantly accept as normal the organs reduced in weight by inanition, thus underestimating both the mean value and the upper limit of normal variation in weight. This source of error is inherent in most pathologic data, since most people are ill for some time before death. Pearl and Bacon [7] discussed this serious limitation of hospital records of necropsies and stated that the ideal subjects for establishing normal standards would be those killed by violent accidents. Since the staff of the department of pathology of the University of Minnesota perform all coroner's autopsies in Hennepin County, which, according to Bell,[9] amount to about 200 a year, the records of the department contain considerable data on the weights of organs from persons killed by violent accidents.

In view of these various considerations, at Dr. Barron's request,[10] I undertook to establish more exactly from these data on accidental deaths the probable upper limit of normal weight of the liver and the spleen, including the age and sex differences and, as a necessary step, the normal variability in weight of the liver and the spleen. Dr. Bell granted the free use of all the records of the department of pathology.

CHARACTER AND SELECTION OF DATA

Of the 9,886 necropsies performed on adults 20 or more years of age from January, 1920, to July, 1931, inclusive, death was due to accidental causes, such as fractured skulls, gunshot wounds, suffocations and poisonings in 1,791, or 18 per cent of the subjects. Records of 175 necropsies were not usable because of incomplete information as to age, body length or weight of the liver and spleen. In addition, 34 records for persons 80 years or more of age were omitted because they were too few for statistical analysis. Of the remaining 1,582 subjects, 1,266 were males and 316 females. Information as to race

9. Bell, E. T.: J. A. M. A. 90:896, 1928.

10. Financial aid for this study was given by a grant made to Dr. Barron of the department of medicine by the Research Fund of the Graduate School of the University of Minnesota.

or nationality was given consistently only when the race could be recognized by pigmentation. According to this criterion, the subjects were predominantly Caucasians, since there were only 31 Negroes and 4 Chinese.

The routine procedure in performing a necropsy is first to open the abdomen and inspect its contents, and then to open the thorax and inspect its contents; next the thoracic organs are removed, and finally, the abdominal organs. Usually the spleen is removed before the liver. If an assistant is present, which is generally the case at coroner's necropsies, the organs are weighed immediately after removal; otherwise they are put aside until the end of the examination, when all organs are weighed. When the autopsy is done at the city morgue, the organs are weighed accurately to 1 Gm. on a counterbalance pan scale. When the examination is conducted in an undertaking establishment, hospital morgue or home, the spleen is weighed on a portable spring balance scale reading to 10 Gm. and the liver is weighed on one reading to 25 Gm. With use the spring stretches, so that the scales tend to read too high. More than 95 per cent of the postmortem examinations are made at the city morgue.

In cases of deaths from accidents, the interval between the time of injury and of death may vary from a few minutes to several weeks. If this period is prolonged, more or less malnutrition usually occurs, which, according to Jackson's summary,[8] reduces the size of the organs, and secondary infections set in, which may either indirectly reduce the weight of the organs by affecting nutrition or directly enlarge the organs by cloudy swelling. To avoid including the weights of organs materially affected either by malnutrition or by secondary infections, I arbitrarily divided the data into two major groups, namely, for persons (I) ill less than twenty-four hours, and (II) ill one day or more. This time limit, first used by Hammar,[11] is the same that I used in a similar analysis of the weight of the thymus,[12] in which the weights were significantly lowered when the subjects had died within from one to seven days after the onset of the illness. Since the thymus is probably more sensitive to inanition than any other organ,[8] this time limit may be assumed to be adequate for eliminating organs which have been affected by inanition and is probably short enough to avoid any marked effects of secondary infections.

While most of the persons killed by accidents were able to work up to the time of injury, some of them were known to be sick or had a

11. Hammar, J. A.: Arch. f. Anat. u. Entwcklngsgesch., supp., 1906, p. 91; Ztschr. f. mikr.-anat. Forsch., supp., vol. 6, 1926; supp., vol. 16, 1929.

12. Boyd, E.: Am. J. Dis. Child. **43**:1162, 1932

latent disease process, which was found at necropsy. As a result, two secondary categories were set up: (*A*) no additional disease, and (*B*) additional disease, as indicated by signs or symptoms of disease present before injury or by evidence of disease found post mortem. When infectious processes were apparently secondary to injury, they were classified as (*A*) no additional disease. Signs of old healed infections, such as pleural adhesions, were not considered disease processes. Also, since arteriosclerosis was found in many subjects over 50 years of age, it was accepted as part of the normal age changes in the body. These two decisions were made after plotting all weights of both organs against age and indicating which ones came from subjects with arteriosclerosis or old healed infections. As judged by inspection of the scatter diagrams, these conditions did not affect the weights of either organ.

Many of the protocols contained the diagnosis of alcoholism, and 98 subjects died of acute alcoholism. Unfortunately, the absence of a statement concerning alcohol does not mean that it was not used, and, on the other hand, the diagnosis of alcoholism gives no index of the amount of alcohol consumed. After graphic analysis of the data, I came to the following conclusions:

When the diagnosis was acute alcoholism and there was no fatty degeneration of the liver, the case might be considered one of acute poisoning. When alcoholism was recorded in a death from an accident and the liver showed no fatty degeneration, the case was considered as a death from accident, i. e., (*A*) no additional disease. Finally, when either chronic alcoholism or a fatty liver was present, the case was considered one of (*B*) additional disease. As a matter of fact, when chronic alcoholism was diagnosed, fatty degeneration of the liver was almost always present.

The character of the agent causing death might materially affect the weights of both the liver and the spleen. Poisons which act directly on the central nervous system, such as strychnine, hydrocyanic acid and morphine, would not be expected to change the weight of either organ materially, while those which act by injuring the parenchymatous organs, such as compounds of mercury, arsenic and bismuth, and the strong acids or caustics, such as phenol, lye and compound solution of cresol, would probably materially affect the weights of the liver and the spleen. Hence the cases of poisonings were separated into these two general groups, and burns were arbitrarily added to the latter group.

When a person is killed by violence, excessive loss of blood frequently occurs and is often the cause of death. Preliminary tests indicated that this loss of blood materially reduced the weights of both the liver and the spleen.[13] The diagnosis of gross hemorrhage was made when the protocol contained such findings as rupture of the liver, spleen, heart, large blood vessels, hemoperitoneum and hemothorax.

Finally, all organs, and especially the spleen, are apt to be congested in subjects killed by electrocution, suffocation or drownings and carbon monoxide poisoning. This congestion was assumed to be within physiologic limits of the organs.

As a result of these considerations, the data within the two categories, (I) ill less than twenty-four hours and (II) ill one day or more, and their subdivisions, (*A*) no additional disease and (*B*) additional disease, were each again subdivided into (1) all accidents without gross hemorrhage, consisting of (*a*) trauma without gross hemorrhage, (*b*) electrocutions, suffocations and drownings, (*c*) poisoning by carbon monoxide, cyanide compounds, alkaloids and narcotics and (*d*) poisoning by alcohol, (2) trauma with gross hemorrhage and (3) poisonings by heavy metals, strong acids and caustics, and burns, as shown in table 1.

The 312 cases falling under the headings (I) ill less than twenty-four hours, (*A*) no additional disease, (1) accidents without gross hemorrhage, may be considered essentially normal subjects; hence a reasonable sample from which to establish standards of normal variability in weights of organs. The 489 cases falling under the headings (I) ill less than twenty-four hours, (*A*) no additional disease, (2) trauma with gross hemorrhage are equally normal subjects. They are comparable to the laboratory animal killed by a blow on the head and then bled by cutting the vessels of the neck, while the group I have considered normal is comparable in part, at least, to the laboratory animal killed by etherization.

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13. The marked effect of gross hemorrhage on these weights was found inadvertently. In the first sorting of the record cards, I had separated those cases with rupture of either the liver or the spleen, with the idea of excluding them from the normal data. Graphic analysis showed that the weights of these ruptured organs fell within the same range as the organs from other cases of trauma, but large numbers of them were in the lower part of the range. Also, if only the livers were ruptured, the nonruptured spleens from the same subjects tended to fall in the same part of the ranges as the weights of the ruptured spleens. The same relation held for the weights of ruptured spleens and nonruptured livers. When the traumatic cases without rupture of either liver or spleen were divided into those with and those without gross hemorrhage from other ruptured organs, the weights from cases without any gross hemorrhage tended to fall above the weights from those with hemorrhage. Moreover, the weights from cases of hemorrhage did not seem to vary according to source of hemorrhage, i. e., the livers and spleens themselves or other organs. Hence it was concluded that massive hemorrhage from any part of the body reduced the weight of the liver and spleen as much as hemorrhage from the organs themselves.

After discussing this problem with me, Dr. Charlotte Van Winkle[14] carried out a comparison of both the weights of the liver and the spleen between guinea-pigs killed by a blow on the head and those killed by etherization. Her findings, which will be published elsewhere, show that the liver is significantly smaller in the group that was bled, while there is no demonstrable difference between the weights of the spleen in this group bled and the group that was killed by etherization. The latter finding is not in agreement with the findings for man, in whom both organs are reduced by gross hemorrhage, as will be demonstrated later. A possible physiologic explanation is that the spleen contracts in the struggling etherized animal, thus emptying the spleen of blood as effectively as by bleeding by cutting the large vessels while the heart

TABLE 1.—*Case Incidence According to Type of Accident Causing Death, Duration of Illness, Presence or Absence of Disease and Sex*

	I. Ill Less Than 24 Hours (1,074 Cases)						II. Ill 1 Day or More (508 Cases)						
	A. No Additional Disease			B. Additional Disease			A. No Additional Disease			B. Additional Disease			
	Male	Female	Both Sexes	Male	Female	Both Sexes	Male	Female	Both Sexes	Male	Female	Both Sexes	Totals
(1) All accidents without gross hemorrhage	239	73	312	121	41	162	145	30	175	149	38	187	836
(2) Trauma with gross hemorrhage	406	83	489	58	12	70	79	13	92	27	7	34	685
(3) Poisonings by heavy metals, burns, etc.	18	5	23	12	6	18	9	5	14	3	3	6	61
Totals	663	161	824	191	59	250	233	48	281	179	48	227	1,582

is still beating. Further consideration of this problem will be taken up by Dr. Van Winkle in her article.

Since most deaths from disease are not associated with gross hemorrhage, the nonhemorrhagic group has been used for establishing normal standards of variability in the weight of the liver and spleen.

ANALYSIS OF DATA

When the weights of the liver and spleen from the nonhemorrhagic group just selected as normal are plotted for both sexes against age (charts 1 and 2), the weights of the liver in both sexes seem to increase slightly from 20 to 50 years of age, especially in the upper range of weight, then to decrease, and the livers of the males tend to be larger than those of the females. On the other hand, the weights of the spleen in both sexes appear to decrease both in amount and variability from 20 to 50

14. Pathologist and Director of Laboratory, Glen Lake Sanatorium, Oak Terrace, Minn.

years, and the weights of the spleen in the females do not appear to be materially smaller than those of the males.

The central trend in weight of these organs could be represented by various methods. The most common procedure in current use is to average the weights for given age periods, then to pass a trend line through these averages by a point to point line drawn in from average

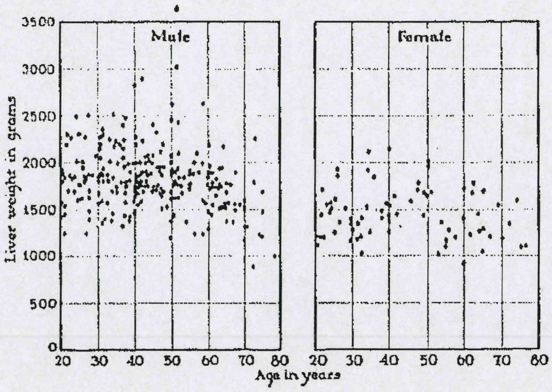

Chart 1.—Scatter diagrams of the weights of the livers with age from normal males and females, i. e., those in the group (I) ill less than twenty-four hours, (*A*) no additional disease, (1) all accidents without gross hemorrhage.

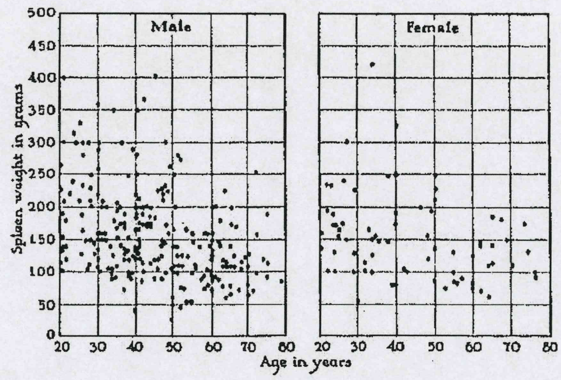

Chart 2.—Scatter diagrams of the weights of the spleen with age from normal males and females, i. e., those in the group (I) ill less than twenty-four hours, (*A*) no additional disease, (1) all accidents without gross hemorrhage.

to average, or by a smooth curve drawn by inspection to the averages, or by fitting a line to the averages by the method of least squares, or, for the weights of the spleen which appear to have approximately a straight line trend with age, by fitting the regression line by the Pearsonian correlation technic. The variability around these trends could be measured in terms of one and two standard deviations from the mean weights for each age period or from the regression line for all age periods, so that the middle two thirds of the weights would fall between plus and minus one standard deviation and the middle 95 per cent of the weights between plus and minus two standard deviations. Actually, these methods were first applied to these data, but it was found that the weights of both organs, and especially those of the spleen, like those of the thymus,[12] were so skew that the lower two standard deviations line fell below all the weights, instead of 2.5 per cent of the weights falling below it.[15]

Construction of Standards of Normal Variability in the Weight of the Liver and the Spleen.—As a result of these findings, as in the analysis of the weights of the thymus, the medium weights,[16] or 50 percentiles of weight for 10 year age periods, were used to represent the central trend; the weight range from the 25 to the 50 percentiles, the middle 50 per cent of the weights, and the weight range from the 10 to the 90 percentiles, the middle 80 per cent of the weights. To these were added the 2.5 and the 97.5 percentiles as the probable lower and upper limits of normal variability.[17]

The designated percentiles were found for the weights of both organs in each 10 year age group for both sexes by the graphic method given by Yule.[18] The values for each percentile along with the minimum and maximum weights for the liver are given in table 2, and for the spleen in table 3. Whenever there were marked irregularities from age period to age period, the values were smoothed by one application of three point smoothing.[19]

15. When the weights were plotted on a six-zone standard based on plus and minus one and two standard deviations, the Chi-square and P for the difference between the observed and theoretical number in each zone were 14.79 and 0.01 for the liver and 27.21 and 0.000057 for the spleen.

16. On the average, in these data the median weight of the liver is in males 24 Gm., or 1.4 per cent below the mean weight, and in females 48 Gm., or 3.3 per cent. The median weight of the spleen is on the average in males 13 Gm., or 8.3 per cent below the mean weight, and in females 10 Gm., or 6.8 per cent. The means, standard deviations and correlations of liver and spleen, liver and height and spleen and height will be published in a subsequent report.

17. These arbitary limits were chosen because they represent essentially the same level of probability, i. e., 0.025, commonly used as the dividing line between probably significant and nonsignificant deviations within a normal distribution. Hence, the 97.5 and 2.5 percentile lines of these skew distributions correspond approximately to plus and minus three probable errors, or two standard deviations from the mean of normal distributions.

18. Yule, G. U.: An Introduction to the Theory of Statistics, ed. 9, London, Charles Griffin & Co., 1929.

19. The weight for the calculated 2.5 percentile can be less than the observed minimum weight when there are few weights and several are near the minimum weight, so that the curve drawn in by inspection extends beyond the minimum weight. The same principle applies when the weight for the 97.5 percentile is larger than the observed maximum weight.

Graphic charts giving the variability for the total age period for each organ and sex were constructed by plotting the weights for the 97.5, 90, 75, 50, 25, 10 and 2.5 percentiles of each 10 year age interval against the mid-age of the interval and by joining all 97.5 percentiles with a continuous line, all 90 percentiles with another continuous line, and so on for the 75, 50, 25, 10 and 2.5 percentiles, respectively.

TABLE 2.—*Percentiles of Weight for the Normal Liver* [19]

Age Interval, Years	Number of Cases	Maximum Weight, Gm.	Percentiles of Weight in Grams							Minimum Weight, Gm.
			97.5	90	75	50	25	10	2.5	
					Males					
20 to 29	38	2,500	2,480	2,300	2,000	1,820	1,640	1,420	1,300	1,235
30 to 39	54	2,515	2,520	2,310	2,030	1,830	1,670	1,490	1,370	1,327
40 to 49	58	2,900	2,600	2,290	2,030	1,840	1,670	1,510	1,350	1,470
50 to 59	39	3,020	2,570	2,190	2,000	1,840	1,640	1,510	1,350	1,200
60 to 69	37	2,400	2,420	2,070	1,890	1,740	1,580	1,420	1,320	1,200
70 to 79	13	2,203	2,140	1,860	1,640	1,380	1,180	1,020	900	900
					Females					
20 to 29	19	1,920	1,900	1,720	1,560	1,440	1,280	1,140	1,080	1,114
30 to 39	14	2,120	2,040	1,820	1,620	1,400	1,320	1,200	1,080	1,023
40 to 49	11	2,130	2,100	1,910	1,690	1,440	1,290	1,180	1,220	1,250
50 to 59	11	2,000	1,990	1,870	1,700	1,420	1,260	1,140	1,010	1,020
60 to 69	13	1,780	1,880	1,780	1,590	1,380	1,150	1,050	910	925
70 to 79	5	1,595	1,760	1,600	1,380	1,180	1,100	1,040	1,000	1,100

TABLE 3.—*Percentiles of Weight for the Normal Spleen* [19]

Age Interval, Years	Number of Cases	Maximum Weight, Gm.	Percentiles of Weight in Grams							Minimum Weight, Gm.
			97.5	90	75	50	25	10	2.5	
					Males					
20 to 29	35	400	364	318	250	194	144	116	96	90
30 to 39	54	360	356	281	220	172	131	106	86	75
40 to 49	58	400	327	234	187	144	112	86	65	76
50 to 59	39	280	285	220	172	135	108	84	61	25
60 to 69	37	225	243	205	147	113	94	74	61	60
70 to 79	13	255	234	188	136	108	90	74	66	65
					Females					
20 to 29	19	300	300	255	205	165	130	95	65	65
30 to 39	14	420	310	258	200	162	118	85	63	55
40 to 49	11	325	293	252	195	142	102	80	65	80
50 to 59	11	250	273	227	182	135	95	77	67	75
60 to 69	13	284	230	198	160	113	87	78	68	61
70 to 79	5	175	195	175	140	110	95	78	70	90

The results are shown in charts 3 and 4, and the scatter of observed values against the standards constructed from them in charts 5 and 6. According to the construction of the graphs, 2.5 per cent of the weights of normal organs would be expected to fall both above the 97.5 percentile line and below the 2.5 percentile line, 7.5 per cent in the clear zones between the 97.5 and 90 and the 10 and 2.5 percentile lines, 15 per cent in the lightly shaded zones between the 90 and 75 and the 25 and 10 percentile lines, and 25 per cent in the heavily shaded zones between both the 75 and 50 and the 50 and 25 percentile lines.

According to these charts and tables, the liver of the male tends to increase from a median weight of 1,820 Gm. at 25 years to a median weight of 1,840 Gm. at 55 years and then to decrease 360 Gm., or 20 per cent, to a median weight of 1,480 Gm. by 75 years. The median

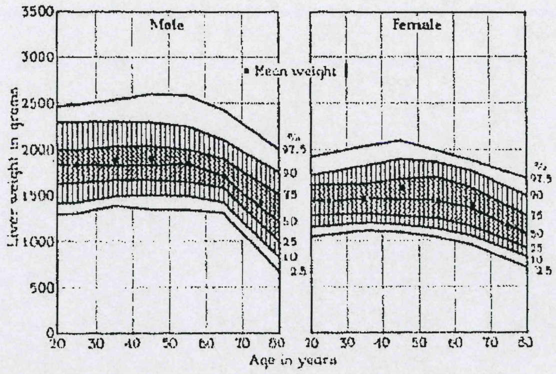

Chart 3.—Graphic standards of normal variability in weight of the liver of both the male and the female based on the data in chart 1. The percentage figures given at the side of each panel indicate the percentiles of weight. Fifty per cent of normal weights may be expected to fall in the heavily shaded zone, 80 per cent in the totally shaded zone and 95 per cent in the total zone limited by the 97.5 and the 2.5 percentile lines. For practical purposes, the last two percentile lines may be considered the usual upper and lower limits of normal variability in weight of the liver.

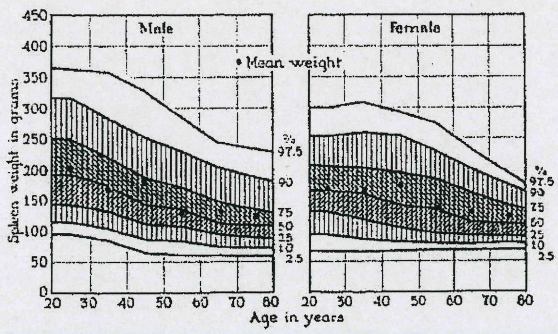

Chart 4.—Graphic standards of normal variability in weight of the spleen of both the male and female based on the data in chart 2. The percentage figures given at the side of each panel indicate the percentiles of weight. Fifty per cent of normal weights will be expected to fall in the heavily shaded zone, 80 per cent in the totally shaded zone and 95 per cent in the total zone limited by the 97.5 and the 2.5 percentile lines. For practical purposes, the last two percentile lines may be considered the usual upper and lower limits of normal variability in the weight of the spleen.

weight of the liver of the female fluctuates between 1,460 and 1,430 Gm. in the four decades from 20 to 60 years, then definitely decreases approximately 250 Gm., or 11 per cent, to 1,180 Gm. by 75 years. Thus, the liver of the male is from 200 to 400 Gm. heavier than the liver of the female, and the liver in both sexes is essentially stationary in weight from 20 to 55 years of age and then decreases in weight.

The variability in the weight of the liver, as illustrated by the various shaded zones, shows that on the average the middle 50 per cent of weights covers a range of 370 Gm. in the male and 360 Gm. in the female, the middle 80 per cent a range of 840 Gm. in the male and 660 Gm. in the female, and the middle 95 per cent a range of 1,190 Gm. in the male and 900 Gm. in the female. In relative terms, the 75 percentile line averages 15 per cent above the median line for males and

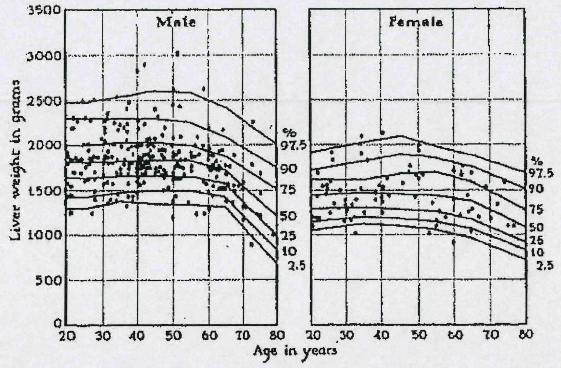

Chart 5.—Graph showing the weights of the liver from normal males and females, chart 1, plotted on the percentile standard, chart 3, constructed from these weights.

11 per cent for females, while the 25 percentile line averages 10 per cent below the median line for both sexes. The 97.5 percentile line averages 42 and 40 per cent above the median line, and the 2.5 percentile line 26 and 24 per cent below it. These findings show the marked skewness of the weights in both sexes and for all age periods.

In contrast to the liver, the spleen in both sexes tends to decrease throughout adult life. The median weight of the spleen of the male decreases 86 Gm., or 44 per cent, from 194 Gm. at 25 years to 108 Gm. at 75 years, and that of the female decreases 55 Gm., or 33 per cent, from 165 Gm. at 25 years to 110 Gm. at 75 years. There is no material difference between the median weights for the two sexes, except in the decade from 20 to 30 years, when the spleen of the male is 14 per cent heavier than that of the female. In the male the middle 50 per cent of weights cover a mean range of 72 Gm., the middle 80 per cent a mean range of 156 Gm. and the middle 95 per cent a mean range of 227 Gm. In the female these ranges are 76 Gm., 146 Gm. and 156 Gm., respectively. Relatively, this variability is about twice that of the liver. In the male the 75 percentile line averages 28 per cent above the median weight, and the 25 percentile line averages 23 per cent below it; the 97.5 percentile line averages 111 per cent above the median weight and the 2.5 percentile line averages 49 per cent below. In the female the 75 and 25 percentile lines average 31 and 23 per cent above and below the median weight, respectively, and the 97.5 and 2.5 percentile lines average 94 and 47 per cent above and below it.

This great normal variability in the spleen, as estimated from these data, is probably due to the normal contractility of the organ. In data

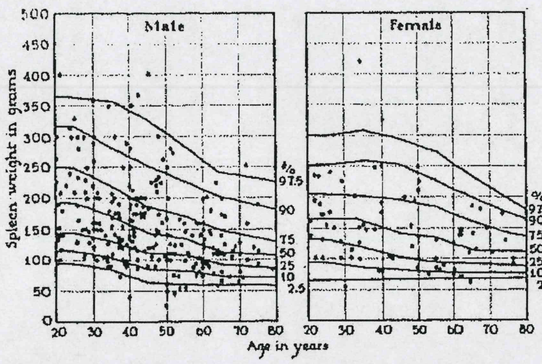

Chart 6.—Graph showing the weights of the spleen from normal males and females, chart 2, plotted on the percentile standard, chart 4, constructed from these weights.

from man, the state of contraction or dilatation cannot be controlled. As a result, the weights of the spleen from conditions known to cause contraction would tend to fall in the lower zones, and those from conditions which cause dilatation would tend to fall in disproportionate numbers in the upper zones of these standards. The latter possibility apparently occurred in the cases of poisoning from carbon monoxide, cyanide and other poisons, since 70 per cent of the weights in this group fell above the median line and only 30 per cent below it, in contrast to the expected 50 per cent on each side of the line.

That this disproportion is more than would be expected to occur by chance alone is demonstrated in the following test of the standard:

The goodness of the fits of the standards to the weights of both the liver and the spleen in the normal group, (I) ill less than twenty-four hours, (*A*) no additional disease, (1) all accidents without gross hemorrhage, and its subdivisions was tested by the Chi-square method. (The steps of this method are illustrated in table 6 for the comparison of the hemorrhagic group with the standard.) The fits for the total and all subgroups, except the weights of the spleen in cases of nonalcoholic poisoning, were found to be excellent, since the probability integrals, P, given in tables 4 and 5 were usually close to 0.90 and never less than 0.22, indicating that the differences could occur from chance alone from twenty-two to ninety times in a hundred.

Commonly, if P is 0.01 or less, i. e., chance could account for such a difference only once in a hundred times, it is assumed that the difference in that given comparison is not due to chance, and this difference is called significant. Hence, since P for the subgroup, poisonings by carbon monoxide, cyanide and other poisons, is 0.003, the 70 per cent of weights of the spleen above the median is significantly above the expected 50 per cent. Pathologists have the impression that relatively large spleens are found in cases of carbon monoxide poisoning. Because of this, I separated on the graphs the weights in cases of poisoning due to carbon monoxide from those due to other poisons. Both groups, however, tend to have a relatively high number of weights in the upper range of the normal variability. Hence, in the persons killed by the poisons which act on the central nervous system, the spleen tends to be larger than in persons killed by trauma. The liver of these same subjects shows no such tendency. Possibly, along with the paralysis of either respiratory or cardiac centers in the central nervous system, the vasomotor control of vessels to the spleen is stopped so that the spleen becomes dilated and filled with blood. On the other hand, in the various types of trauma, death has taken place with the spleen in any phase of its possible physiologic range from marked contraction to extreme dilatation.

On the whole, these standards may be assumed to be reasonable estimates of the central trend of the weights of the liver and the spleen with age and the variability around that central trend. The standard for males is more reliable for both organs than that for females, because the basic sample consisted of four times as many cases. Also the standards for the liver are more reliable than those for the spleen, because of the great physiologic variability of the spleen. The 97.5 and 2.5 percentile lines may be assumed to represent the probable limits of normal size, although two or three weights in every hundred in this series fell above and below these lines, and the same number would be expected in another identical series. However, the likelihood is great that the extreme upper and lower weights in this series actually came from subjects with some pathologic condition which was not recognized at postmortem examination or which did not leave adequate signs to be recognized by the customary methods of making the examinations.

TABLE 4.—*Comparison of the Weights of the Liver in the Various Subdivisions of the Normal Group (I) Ill Less Than Twenty-Four Hours, (A) No Additional Disease, (1) All Accidents Without Gross Hemorrhage, With the Normal Standard*

	Sex	Number of Weights	Percentage of Weights: Above 97.5 Line	Between the Percentile Lines: 97.5 to 90	90 to 75	75 to 50	50 to 25	25 to 10	10 to 2.5	Below 2.5 Line	n′	χ^2	P	Percentage of Weights: Above 50 Line	Below 50 Line
Percentage of weights expected			2.5	7.5	15	25	25	15	7.5	2.5				50	50
(1) All accidents without gross hemorrhage	Male	239	3	6	16	26	24	16	6	3	6	0.56	0.96	51	49
	Female	73	3	10	12	23	29	12	7	4	4	0.59	0.80	48	52
	Both sexes	312	3	6	15	26	25	15	6	4	6	0.08	0.99	50	50
(a) Trauma without gross hemorrhage	Male	102	4	1	15	27	20	17	12	4	6	7.18	0.22	47	53
	Female	44	5	11	13	23	23	11	9	5	4	0.55	0.80	52	48
	Both sexes	146	4	4	15	26	21	15	11	4	6	5.14	0.42	49	51
(b) Electrocutions, suffocations and drownings	Both sexes	45	4	7	20	13	31	20	3	2	4	3.80	0.26	44	56
(c) Poisoning by carbon monoxide, hydrocyanic acid, etc.	Both sexes	73	2	7	7	33	32	14	1	4	4	6.17	0.11	49	51
(d) Poisoning by alcohol	Both sexes	48	0	15	23	25	21	10	4	2	4	4.07	0.17	63	37

TABLE 5.—*Comparison of the Weights of the Spleen in the Various Subdivisions of the Normal Group, (I) Ill Less Than Twenty-Four Hours, (A) No Additional Disease, (1) All Accidents Without Gross Hemorrhage, With the Normal Standard*

	Sex	Number of Weights	Percentage of Weights: Above 97.5 Line	Between the Percentile Lines: 97.5 to 90	90 to 75	75 to 50	50 to 25	25 to 10	10 to 2.5	Below 2.5 Line	n′	χ^2	P	Percentage of Weights: Above 50 Line	Below 50 Line
Percentage of weights expected			2.5	7.5	15	25	25	15	7.5	2.5				50	50
(1) All accidents without gross hemorrhage	Male	239	2	8	15	26	23	15	8	3	6	0.55	0.96	51	49
	Female	73	6	1	19	22	23	18	8	3	4	0.81	0.85	48	52
	Both sexes	312	3	6	16	25	23	16	8	3	6	1.20	0.96	50	50
(a) Trauma without gross hemorrhage	Male	102	1	8	13	25	25	18	8	2	6	0.99	0.95	47	53
	Female	44	4	0	16	21	25	18	11	5	4	2.18	0.60	41	59
	Both sexes	146	2	5	14	24	25	18	9	3	6	2.28	0.85	45	55
(b) Electrocutions, suffocations and drownings	Both sexes	45	2	5	20	29	22	18	2	2	4	3.28	0.80	56	44
(c) Poisoning by carbon monoxide, hydrocyanic acid, etc.	Both sexes	73	7	12	22	29	15	10	4	1	4	13.74	0.003	70	30
(d) Poisoning by alcohol	Both sexes	48	0	2	12	19	29	17	17	4	4	6.17	0.11	33	67

Every pathologist is familiar with the case in which an obviously ill patient dies but no cause of death can be found. Moreover, in this series the coroner's records are apt to be incomplete concerning symptoms previous to injury.

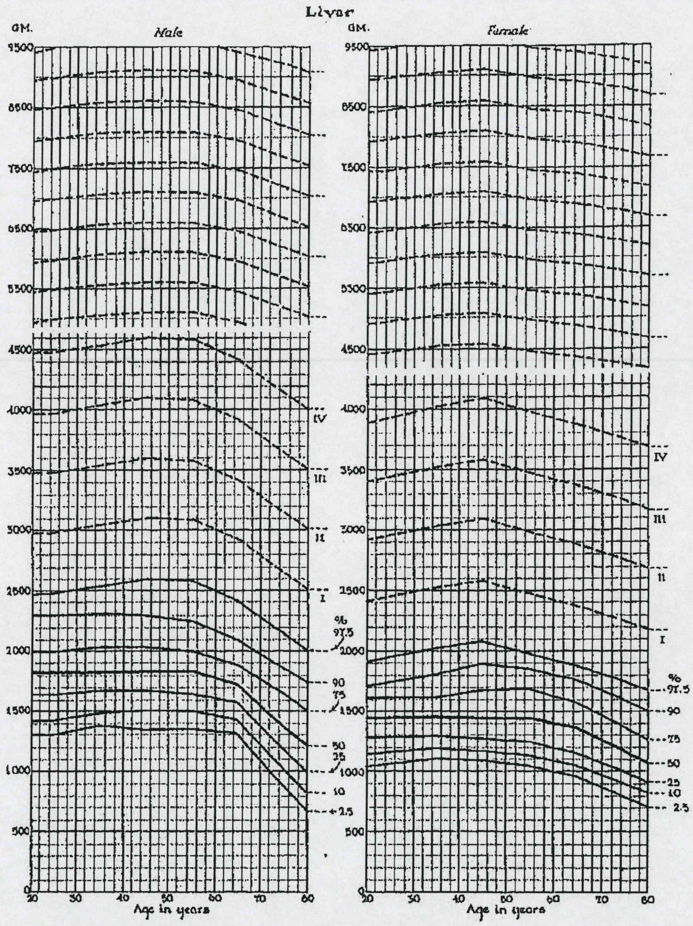

Chart 7.—Work chart of 500 Gm. zones of hypertrophy of the weight of the liver of both the male and the female superimposed above the 97.5 percentile lines of chart 3. Above zone IV the scale was reduced in order to include a sufficient number of zones for pathologic weights.

Zones of Hypertrophy.—In order to make the standards of normal variability useful for Dr. Barron's purposes, namely, degree of hypertrophy of the liver and the spleen in various disease conditions, zones of 500 Gm. for the liver and 100 Gm. for the spleen were drawn in above the 97.5 percentile line, as shown in charts 7 and 8. Inspection of chart 3 or 7 indicates that the estimate of the upper limit of the normal weight of the liver at 2,200 Gm. made by Barron and Litman [1] would have included approximately from 10 to 15 per cent of the livers of normal males, and especially those of men under 60 years of age,

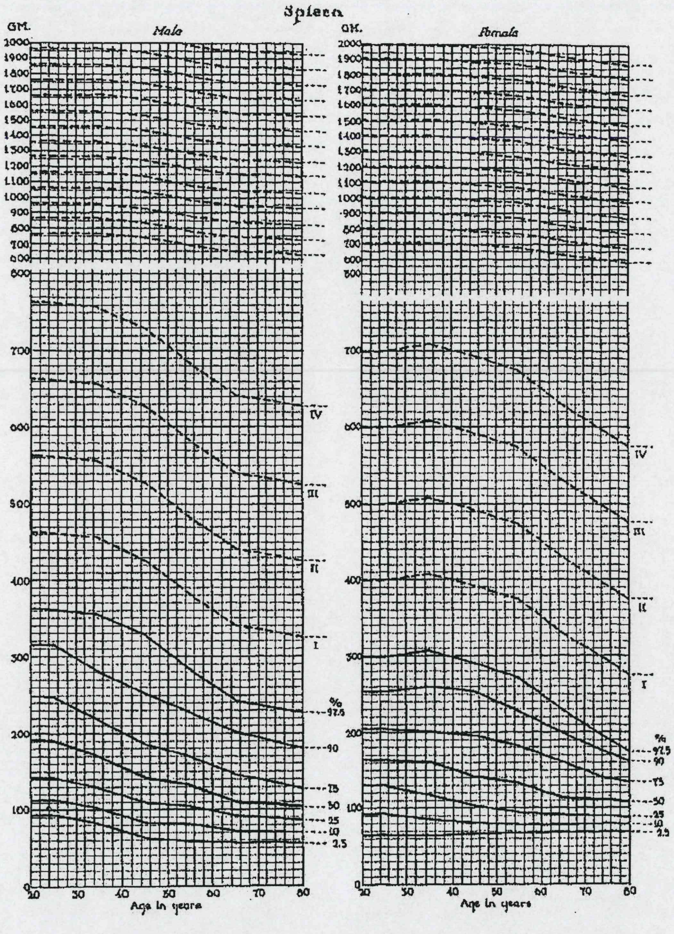

Chart 8.—Work chart of 100 Gm. zones of hypertrophy of the weight of the liver of both the male and the female superimposed above the 97.5 percentile lines of chart 4. Above zone IV the scale was reduced in order to include a sufficient number of zones for pathologic weights.

while certain hypertrophied livers in females would not have been considered enlarged. Inspection of charts 4 and 8 shows that their estimate of 300 Gm. for the upper limit of the normal weight of the spleen would include as hypertrophied about 10 per cent of the spleens in normal young men and a few of those of young women, while after middle age certain hypertrophied organs would not have been included in their series. This would indicate, on the basis of their assumption that spleens weighing 300 Gm. and livers weighing 2,200 Gm. are palpable, that about 15 per cent of the livers of healthy mature men are palpable and about 10 per cent of the spleens of young men are palpable. This fits with the common clinical practice of accepting, in the absence of symptoms, a just palpable liver or spleen as probably normal. Since they were interested primarily in the very large livers and spleens, weighing 4,000 and 550 Gm., respectively, these findings will not affect their analysis of the importance of hepatomegaly and splenomegaly in differential diagnosis.[20]

Comparison of the Data for Accidental Deaths, Which Were Not Used in Establishing the Standard, With the Normal Standard.—The effect of gross hemorrhage on the weight of both organs is shown in charts 9 and 10, in which the weights from the hemorrhagic group, (1) ill less than twenty-four hours, (*A*) no additional disease, (2) trauma with gross hemorrhage, are plotted on the standards. On inspection, a disproportionate number of weights of both organs seems to fall in the lower zones of normal variability, indicating that massive hemorrhage shortly before death materially lowers the weight of both the liver and the spleen. Whether or not this disproportion is due to chance in sampling or to the gross hemorrhage has been tested by Chi-square in the same manner as the standard was tested.

The steps in calculating Chi-square for the weights of the liver in males are illustrated in table 6. The value of P for a given number of zones, n', and the value of Chi-square obtained may be found in Elderton's tables of Chi-square (Pearson),[21] in a nomogram given by Dunn [22] and in Fisher's tables of Chi-square,[23] when n equals (n' —1). For weights of livers of the male the Chi-square of 354 is so great that such deviations from the expected number in each zone would not occur by chance once in a million times, since P is less than 0.000000.

20. Dr. Barron will report later on hypertrophy of the liver and spleen as measured by these standards. We hope ultimately to present a compromise by rank correlation of the interrelation between variability of both organs in the same disease conditions.

21. Pearson, Karl: Tables for Statisticians and Biometricians, ed. 2, London, The Biometric Laboratory, University College, 1924, pt. 1.

22. Dunn, H. L.: Physiol. Rev. 9:275, 1929.

23. Fisher, R. A.: Statistical Methods for Research Workers, ed. 3, London, Oliver & Boyd, 1930.

As stated before, in common statistical practice a P of 0.01,[24] indicating that chance could cause such a difference only once in a hundred times, is considered adequate evidence of a real difference between two samples. Hence the liver of the female and the spleen of both the male and the female in the hemorrhagic group are also significantly different from the standard, because their P's are 0.003, 0.000000 and 0.000000, respectively. Since these differences, as illustrated in charts 9 and 10 and

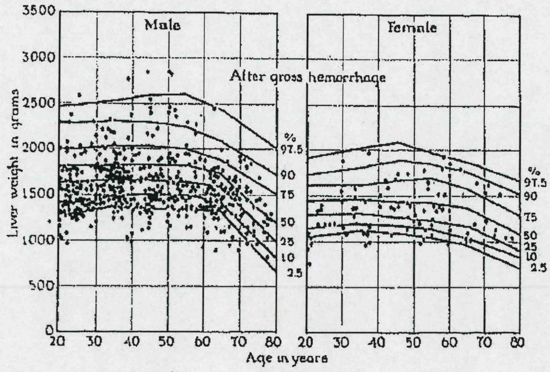

Chart 9.—Graphs showing the weights of the livers from normal males and females dying of trauma with gross hemorrhage plotted on the standards of normal variability of liver weight, chart 3.

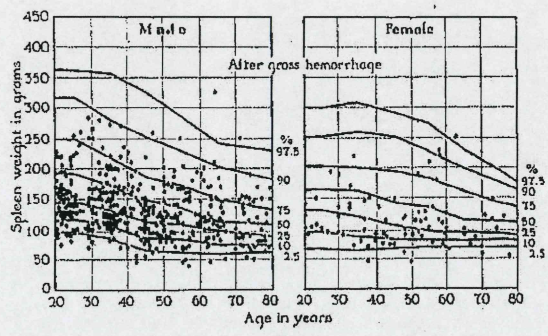

Chart 10.—Graphs showing the weights of the spleen from normal males and females dying of trauma with gross hemorrhage plotted on the standards of normal variability of spleen weight, chart 4.

24. For the convenience of those who do not have the statistical tables at hand, the following table gives the values of Chi-square for a given number of zones, n', at which P is 0.01:

n'	8	6	4	2
χ^2	18	15	11	9

tables 7 and 8, consist of a general lowering of the weights, the interpretation is made that massive hemorrhage materially lowers the weight of both the liver and the spleen.

In like manner, the weights for the other groups excluded from the normal data for accidental deaths listed in table 1 were compared with the standard and the findings summarized in tables 7 and 8. Since fatty degeneration of the liver causes marked hypertrophy, this group for the liver was separated from the groups in which additional disease was present. Also the number of weights in comparable zones of the standards for the males and the females were combined, because no sex differences in the distribution of the weights on the standard were

TABLE 6.—*The Chi-Square Method of Comparing Observed with Theoretically Expected Number of Weights in Each Zone of the Normal Standard*

	Percentile Zones								
	Above 97.5 Line	97.5 to 90 Line	90 to 75 Line	75 to 50 Line	50 to 25 Line	25 to 10 Line	10 to 2.5 Line	Below 2.5 Line	Totals
Expected percentage of weights	2.5	7.5	15	25	25	15	7.5	2.5	100
Expected number of weights, T	10.15	30.45	60.90	101.50	101.50	60.90	30.45	10.15	406
Observed number of weights, O*	5	14	28	53	82	88	77	59	406
T — O	+5.15	+16.45	+32.90	+48.50	+19.50	—27.10	—46.55	—48.85	0
$(T - O)^2$	26.52	270.60	1082.41	2352.25	380.25	734.41	2166.90	2386.32	
$(T - O)^2/T$	2.61	8.89	17.77	23.17	3.75	12.06	71.16	235.11	374.52

χ^2 = sum of $(T - O)^2/T = 374.52$
n' of Elderton's table of χ^2 = number of zones = 8 $\therefore$ P = 0.000000

* Example: The hemorrhagic group, (1) ill less than twenty-four hours, (A) no additional disease, (2) trauma with gross hemorrhage, weights of 406 livers from males, shown in the first panel of chart 9.

demonstrable for any disease. Whenever the combining of the numbers of the sexes did not increase the number expected in the end-zones to ten, the zones were combined until at least that many were expected, and then Chi-square was calculated for the resulting reduced number of zones, 6, 4 or 2, as indicated by the values of n' in the tables.[24]

Study of the tables indicates that when disease was present at time of injury, the variability was usually significantly increased, i. e., a disproportionate number fell in the extreme upper and lower zones, and when illness had lasted more than one day, an increased number of weights of livers fell in the lower ranges, but the weights of spleens showed no significant deviation from the normal. The latter findings are in agreement with Jackson's summary[8] of the effects of inanition on both the liver and the spleen, namely, that both are reduced, but the reduction of the spleen cannot be demonstrated as early in inanition as

TABLE 7.—*Comparison of the Weights of the Liver From the Accidental Deaths, Not Used in Establishing the Standard, With the Normal Standard*

	Number of Weights for Both Sexes	Percentage of Weights: Above 97.5 Line	Percentage of Weights: Between the Percentile Lines: 97.5 to 90	90 to 75	75 to 50	50 to 25	25 to 10	10 to 2.5	Below 2.5 Line	n′	χ^2	P	Percentage of Weights: Above 50 Line	Below 50 Line
Percentage of weights expected		2.5	7.5	15	25	25	15	7.5	2.5				50	50
(1) Accidents Without Gross Hemorrhage														
(I) Ill less than 24 hours:														
(B) Additional disease	97	9	11	11	23	20	15	5	6	6	11.32	0.05	54	46
(C) Fatty liver	65	26	12	28	20	8	4	0	2	4	61.70	0.00	86	14
(II) Ill 1 day or more:														
(A) No additional disease	175	2	6	13	22	22	19	9	7	6	11.95	0.04	43	57
(B) Additional disease	130	9	14	14	14	20	14	10	5	6	32.90	0.00	51	49
(C) Fatty liver	57	25	31	12	14	11	7	0	0	4	57.88	0.00	82	18
(2) Trauma With Gross Hemorrhage														
(I) Ill less than 24 hours:														
(A) No additional disease	489	1	4	8	13	22	20	17	15	6	302.51	0.00	26	74
(B) Additional disease	47	4	5	4	13	19	19	21	15	4	23.55	0.00	26	74
(C) Fatty liver	23	13	9	17	22	26	0	4	9	2	1.08	0.30	61	39
(II) Ill 1 day or more:														
(A) No additional disease	92	2	2	12	22	20	17	11	14	6	26.03	0.00	38	62
(B) Additional disease	25	0	0	12	36	8	32	8	4	2	0.04	0.80	48	52
(C) Fatty liver	9	..	..	..	..	..	..	..	..	..	....	....	78	22
(3) Poisoning with Heavy Metals														
(I) Ill less than 24 hours:														
(A) No additional disease	23	0	4	13	9	26	35	9	4	2	2.13	0.15	26	74
(B) Additional disease	15	0	0	20	13	20	20	13	14	..	....	....	33	67
(C) Fatty liver	3	..	..	..	..	..	..	..	..	..	....	....	..	..
(II) Ill 1 day or more:														
(A) No additional disease	14	0	21	22	14	14	22	7	0	..	....	....	57	43
(B) Additional disease	6	..	..	..	..	..	..	..	..	..	....	....	..	..

Table 8.—*Comparison of the Weights of the Spleen From the Accidental Deaths, Not Used in Establishing the Standard, With the Normal Standard*

	Number of Weights for Both Sexes	Percentage of Weights: Above 97.5 Line	Between the Percentile Lines: 97.5 to 90	90 to 75	75 to 50	50 to 25	25 to 10	10 to 2.5	Below 2.5 Line	n′	χ^2	P	Percentage of Weights: Above 50 Line	Below 50 Line
Percentage of weights expected		2.5	7.5	15	25	25	15	7.5	2.5				50	50
(1) Accidents Without Gross Hemorrhage														
(I) Ill less than 24 hours:														
(B) Additional disease	162	7	8	13	18	22	16	7	9	6	14.00	0.02	46	54
(II) Ill 1 day or more:														
(A) No additional disease	175	3	8	12	24	26	13	8	6	6	4.23	0.55	47	53
(B) Additional disease	187	10	9	19	17	21	12	9	3	6	22.84	0.00	55	45
(2) Trauma With Gross Hemorrhage														
(I) Ill less than 24 hours:														
(A) No additional disease	489	1	1	11	16	29	23	13	6	6	112.49	0.00	29	71
(B) Additional disease	70	5	6	9	14	30	16	10	10	4	7.83	0.05	34	66
(II) Ill 1 day or more:														
(A) No additional disease	92	3	5	17	19	23	23	7	3	4	6.01	0.11	44	56
(B) Additional disease	34	3	9	6	17	22	21	9	3	2	2.94	0.10	35	65
(3) Poisoning with Heavy Metals														
(I) Ill less than 24 hours:														
(A) No additional disease	23	0	4	17	18	22	35	4	0	2	1.08	0.30	39	61
(B) Additional disease	18	0	6	22	22	22	22	6	0	..	....	....	50	50
(II) Ill 1 day or more:														
(A) No additional disease	14	7	7	7	29	36	7	7	0	..	....	....	50	50
(B) Additional disease	6	..	..	..	..	..	..	..	..	..	....	....	..	..

can the reduction of the liver. They also indicate why the older standards are lower than those presented here, and the age changes are different, even when care was taken to exclude all directly diseased organs (Greenwood,[3] Greenwood and Brown,[4] Bean and Baker,[6] and Bean [6]).

COMMENT

The chief value of the charts presented here as standards of the normal weight of the liver and the spleen, over and above the means with their standard errors for age periods, is that they make it possible to compare a small series of cases from both sexes and covering the total adult age range without any subdivision of the data. In many disease conditions a series of 50 cases is large. If this group has to be divided into two sex groups, then into two or three age groups, the various groups become too small for reliable statistical comparison of the means. Moreover, the weights for a given disease can be plotted on the standards, as the data are gradually collected and an impression of the age and sex trend of the weight of the liver and the spleen in that disease gained before sufficient data are collected to justify the tedious calculations of means and standard deviations.

In using these charts it should be remembered that associated massive hemorrhage will lower the weights; that in wasting diseases most organs are reduced in weight; that if death in a given disease usually occurs with the spleen dilated, the weights will tend to fall in the upper zones, and conversely, if death consistently occurs with the spleen contracted, the weights will tend to fall in the lower zones; that while the 97.5 percentile line may be considered an approximation of the upper limit of normal variability, two to three weights in every hundred of weights in normal subjects, as can be judged by ordinary pathologic diagnosis, will be expected to fall above this line, and that the standards for females are not highly reliable, owing to the small number of cases.

SUMMARY

1. Graphic standards of the normal variability in the weight of both the liver and the spleen for both sexes for the age period from 20 to 80 years have been presented. These standards were constructed from the weights of livers and spleens from persons dying within twenty-four hours of injury, of trauma without any associated gross hemorrhage, of suffocation, of drowning, of electrocution or of poisonings by such substances as carbon monoxide, narcotics, hydrocyanic acid, strychnine and alcohol, and having no history of illness or any disease demonstrable at necropsy except moderate arteriosclerosis and such evidence of old healed infections as pleural adhesions.

2. When compared with these standards, the weights of both the liver and the spleen were materially reduced in persons dying of trauma accompanied by massive hemorrhage.

3. From these charts the deviation of the weights of the liver or the spleen in a given disease condition from the normal range of weights may be determined by plotting the weights on these standards and testing for the significance of the deviation of the observed from the expected number by the Chi-square method.

4. To these standards of normal variability in weight there have been added for the liver 500 Gm. zones of degrees of hypertrophy, and for the spleen, 100 Gm. zones.[25]

25. Photolithic reproductions of charts 7 and 8, such as are being used in Dr. Barron's study, can be obtained at cost (approximately $5 for 200 charts) by writing to the author. If preferred, similar charts may be constructed on any desired scale from tables 2 and 3.