

## UNCERTAINTIES IN GERIATRIC DATA. II. ORGAN SIZE

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As known for many years, and discussed in a preceding paper (1), the complexity of human survival is in part inherent and in part environmental. In measurements of senescence, it is difficult to determine the age at which the decline begins and indeed we have little in the way of markers to determine what is early life and what is late life, or their relationships. Furthermore, there are no sharp divisions in the eras of the living individual. Even those processes that appear to be linear with time, when interpolated or extrapolated, often become complex curves, continuous from gestation to death.

In this paper is presented, in tabular (Table 1) and graphic form (Figs. 1-5), the material from 400 autopsies on patients of various ages. It is pointed out how specific uncertainties apply to autopsy material, making it difficult to draw firm conclusions that can be used productively in a predictive or interpretive manner in a study of human senescence. This material represents all of the autopsies (in 80 per cent of deaths) performed in a Veterans Administration Neuropsychiatric Hospital since it opened seventeen years ago. The data are probably modified in unrecognized ways by the hospital environment. The autopsy values presented here extend and agree with those of literature summaries in tabular form (2). The organ weights are presented in terms of absolute weights and also as percentages of the body weights. Body height and weight were less in older patients, as reported elsewhere (2).

### SELECTION AND NORMALCY OF MATERIAL

In this study, all autopsy cases were included. Arbitrary rejection of material is open to serious question, though this has often been done in studies reported in the literature (3). Since people die in progressively greater numbers with age and thus death rates are generally age-related, how can one justify the rejection of material by gross or even microscopic examination? In examination of the heart at autopsy, for example, it hardly seems wise to reject those hearts that have valvular or other gross deformities. This is particularly true because of the fact that rheumatic heart disease and autoimmune reactions are closely related. The autoimmune theory of aging (4) is thus completely rejected when one rejects deformed valves as a cause of death upon examination of autopsy material concerned with the aging process.

The usual concept of "normal" old people is erroneous. It is true that in late life some persons show fewer changes than others. This, however, does not justify the rejection of those patients who have infirmities, diseases, or have died.

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TABLE 1  
*Organ Size and Age of Subject—Absolute Weights (Average) and Percentages of Body Weights (BW); Vascular Widths*

	Age 20's		Age 30's		Age 40's		Age 50's		Age 60's		Age 70's		Age 80's		Age 90's	
	Avg.	% BW														
Age (yrs)	25.4		35.2		45.2		56.0		64.5		73.3		83.8		92.0	
Adrenal R & L (gm)	24.8	.03	15.3	.02	15.4	.02	25.1	.04	16.7	.02	19.6	.03	14.6	.02		
Aorta, abd. (width mm)	30.5		33.5		38.3		42.2		42.4		52.0		48.8		48.0	
Aorta, thor. (width, mm)	37.0		46.5		51.0		52.1		53.8		61.3		65.8		55.0	
Brain (gm)	1325	1.8	1399	1.8	1233	1.8	1350	2.1	1300	1.9	1270	2.0	1198	1.8		
Heart (gm)	345	.46	466	.59	429	.62	425	.65	444	.64	463	.72	369	.56	390	.64
Kidney, L (gm)	177	.24	200	.26	186	.27	180	.28	177	.26	149	.23	145	.22	110	.18
Kidney, R (gm)	163	.22	181	.23	174	.25	166	.25	173	.25	146	.23	138	.21	105	.17
Liver (gm)	1855	2.5	1929	2.5	1662	2.4	1625	2.5	1569	2.3	1398	2.2	1273	1.9	1000	1.6
Lung, L (gm)	513	.68	601	.77	572	.83	605	.93	575	.83	539	.83	612	.93	690	1.1
Lung, R (gm)	525	.7	780	.99	634	.92	692	1.1	706	0	640	.99	722	1.1	690	1.1
Pancreas (gm)	96.8	.13	113	.14	108	.16	116	.18	112	.16	105	.16	103	.16	110	.18
Pituitary (gm)*	0.6	.8	0.5	.64	.77	1.1	.734	1.1	.72	1.0	.69	1.1	.7	1.1		
Prostate (gm)	22.3	.03	46.3	.06	28.0	.04	26.2	.04	40.6	.06	52.9	.08	50.4	.08		
Spleen (gm)	199	.27	214	.27	157	.23	164	.25	184	.27	138	.21	120	.18	95	.16
Testes (L & R) (gm)			35.7	.05	32.3	.05	40.8	.06	42.1	.06	45.3	.07	32.9	.05		
Thyroid (gm)			25.5	.03	23.2	.03	53	.08	32.6	.05	26.2	.04	29.5	.05		
Ventricle wall, L (mm)	16		16.9		17		18.2		18.5		17.9		18.8		17	
Ventricle wall, R (mm)	3.6		3.7		3.7		4.6		4.9		4.6		3.8		3	
Height (ins.)	69.1		70.1		67.9		67.5		67.3		66.1		66.2		64.5	
Weight (lbs.)	165		173		152		144		153		143		145		135	

\* Percentage of body weight,  $\times 10^{-3}$ .

tional capacities that are closer to those of age 40 or 50, and are capable of self-care and self-maintenance, proves only that such individuals can be found. When it is considered that 80 per cent of the persons who were born at the time this 80-year-old group was born have died, those that have died are just as important to our understanding of senescence and survival as are those who have survived. If we define normal as the behavior of the majority or the average, then it is obvious that when 80 per cent of the members of a group have died, the average member is dead and thus the normal one is dead. This raises serious question as to what we have established by seeking out patients who are capable of projected biologic efficiency in late life. Again, apparently all that such selection establishes is that certain persons are capable of prolonged bio-

logic efficiency in some unknown and uncontrolled fashion. What is more important is an answer to the question, *Why did the others die?*

Therefore, it would seem that in the consideration of senescence and survival in relationship to autopsy data, none of the material can be rejected, since all of the persons who die (including the autopsy cases) are part of the original group, a few of whom may survive into late life. A complete examination of material without regard to age or cause of death is the only way to collect data that eventually will lead to an understanding of the decline, senescence and death of the human.

Models that demonstrate senescent changes are open to similar criticism. Although models are sorely needed, no satisfactory ones have been made available. Thus, to compare the human with other animals without due recognition of the assumptions made, is to introduce additional errors. A lack of knowledge of the lower forms of life makes this even more obvious. We know the survival pattern of few mammals other than man. In fact, we may not know any, when it is considered that in order to know such survival patterns it has been necessary to place the subjects under unusual, confined environments. Even the laboratory mouse and rat present this problem. For example, the fact that the rat has a more uniform relationship between organ size and body size (5) introduces an insurmountable variation from the human for purposes of critical comparison.

#### LACK OF CONTINUITY IN AUTOPSY MATERIAL

One of the principal problems in interpreting material from autopsies is the lack of continuity. In an autopsy subject it is difficult to tell, regardless of the cause of death, whether this person died from sheer chance of stress or from the progression of some type of inherent difficulty. It is apparent that so-called accidents, for example an auto accident, may result from biologic failure of the driver—poor judgment with respect to entering the car, the use of the car, and the particular errand on which he is going, or his biologic inability to withstand the impact of the subsequent physical events. When these aspects are considered, immediately it becomes obvious that it is impossible to discriminate between death due to inherent biologic failure and death due to the environment or to a combination of the two factors.

Let us consider pneumonia in the aged. Some specific event is usually assigned as the predisposing or etiologic factor. For instance, the feeble patient may aspirate food, become "exposed" to a severe environmental influence such as cooling of the body, or come in contact with someone else with the disease; there also may be no apparent cause. In any event, the patient undoubtedly has had all of these experiences before in life. Why does he die this time, at a fixed age? The answer is not simple. Was this experience different from his past experiences or had he some type of progressive inherent cellular failure which no longer could resist the stress, and thus death ensued? Had this patient become unable to respond to the need for adequate antibody production, or did biologic failure precede the invasion by an organism assigned as the cause?

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This makes it doubly difficult to carry over the interpretation from one individual to another in the interpretation of geriatric sequences. If one examines the data on brain weight in Table 1, it may be seen that there is a general trend toward shrinkage with age. Immediately, the question arises: Was this the result of the passage of time, or was it secondary to some vascular change or other fluid imbalance? However, for subjects in their 80's the brain weight of 1198 gm is open to question in comparison with the other ages, since it is known that certain fluid shifts occur in late life, involving loss of water (6) and ions. Therefore, does this loss of weight represent a loss of functional material of the brain, or does it simply represent a loss of fluid which is not related specifically to function? Other evidence (6) appears to substantiate the view that the percentage of dry matter is the same throughout life. When the data are considered on the basis of percentage of body weight, the brain does not decrease in size. Further perusal of Table 1 will raise the same questions in every case. The questions are: Did the person die early because of the size of the particular organ or did he die because the organ could not adapt in the way the others adapted in later life? Did the organ change and result in his death, or was the change the result of the processes that killed the patient?

No attempt is made here to analyze the cause of death. The cause of death seems of little importance from our point of view, except in consideration of certain types of individuals. In considering a few of the specifics of our data, it is noteworthy that we cannot be certain of cause and effect.

In Figure 1, if one examines the data on the widths of the abdominal and

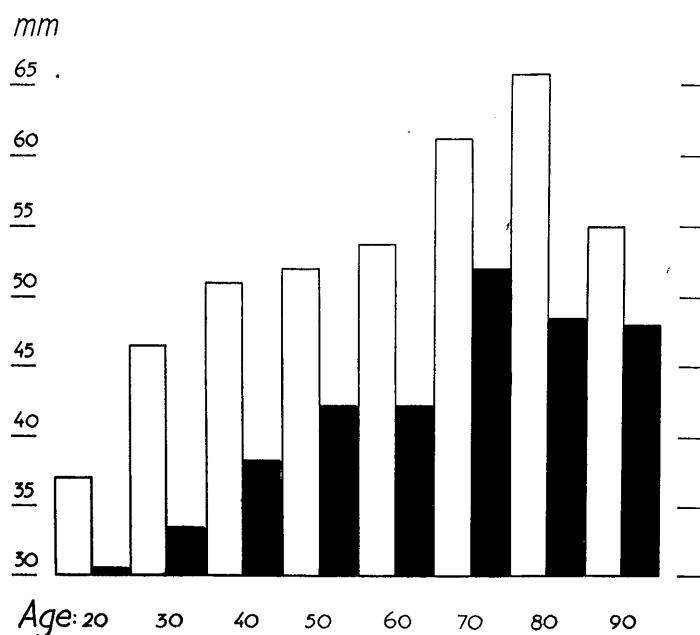


FIG. 1. Changes in width of abdominal aorta (black columns) and thoracic aorta (white columns) with aging.

thoracic aortas in relation to age, one is struck immediately by the fact that there is a widening of the aorta with time. Starting at age 20, the width of the abdominal aorta gradually increased with age up to 70 years. The same was true of the thoracic aorta, although it was constantly larger than the abdominal aorta. After age 70–80 years, the aortas decreased in size, but the change started earlier in the abdominal aorta. One interpretation might be that the aorta became smaller after age 70. This would be most unusual, and it is highly improbable that this process of narrowing occurred. An alternate interpretation is that the aorta remained small in persons who survived to age 80 or 90, which is perhaps more nearly the truth. However, there is a confusing third possibility—that the aortas of the persons who survived to advanced age (particularly to age 90) were inherently made of such material that, as time went on, these aortas *could not* dilate. But then one has to speculate about diet, experience, environment, trauma, blood pressure, employment, and many other factors that might alter the width of the aorta. We are still left with this difficulty of interpretation: Did the person live longer because his aorta was smaller, or did his aorta in some way shrink to a smaller size?

Figure 2 illustrates exactly the same problem. This chart shows the thickness of the walls of the heart. It is obvious that, with time, the left ventricle thickened. It is also of interest that the right ventricle thickened a great deal more than the left. Here again, we are faced with the problem of interpretation. The left ventricle thickened, but the survivors to age 90 had a thinner left ventricle;

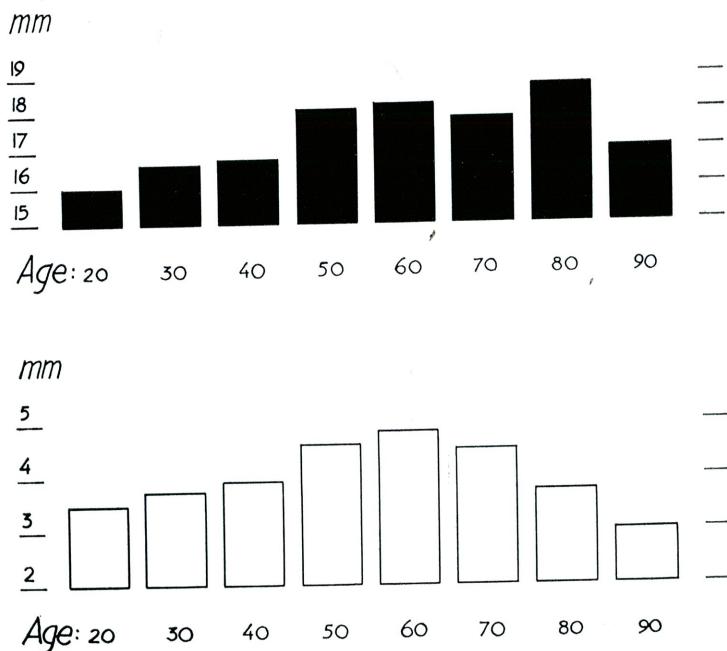


Fig. 2. Changes in thickness of cardiac ventricle walls with aging. Left ventricle, black columns; right ventricle, white columns.

ely by the fact that at age 20, the width of the heart was greater than the abdominal size, but the change in might be that the heart was smaller, and it is highly probable that the alternate interpretation is correct. At age 80 or 90, which rules out the confusing third possibility of a diseased heart (particularly if time went on, these factors about diet, experience, and many other factors that contribute to this difficulty of interpretation. The heart was smaller, or did

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in fact, its thickness was approximately that in a 40-year-old. Was this the result of complete adaptation so that there was no need for the heart to thicken? Does this mean that the heart thickened in those persons in whom there was some obstruction to the outflow and that this hastened their death at an earlier age than in the 90-year-olds? Or does it mean that the person who became 90 simply could not respond and therefore was in some way protected by the fact that his heart did not thicken. Also there is the less probable situation—did the heart become smaller with time and thus adapted to the decreased circulatory needs of the aging subject? The same reasoning applies to the right ventricle. Here it will be seen that there was a more uniform relationship between ventricle thickness and age; the heart wall thickened up to age 60 years and then there was a tendency of the right ventricle to be thinner. But again, exactly what does it mean? Did the ventricles thin out, were they unable to thicken in the persons who lived longer, or were they in such condition that there was no obstruction to the flow of blood through the lungs and therefore no need for the right ventricle to thicken?

It would appear that thickness of the right ventricle is a good method of assaying senescence. Unfortunately, there are no accurate methods of measuring this thickness in the intact human. These questions only emphasize our uncertainty.

When we consider the liver (Fig. 3), there is a similar problem. The liver increased in absolute weight up to age 30, and from then on it became smaller

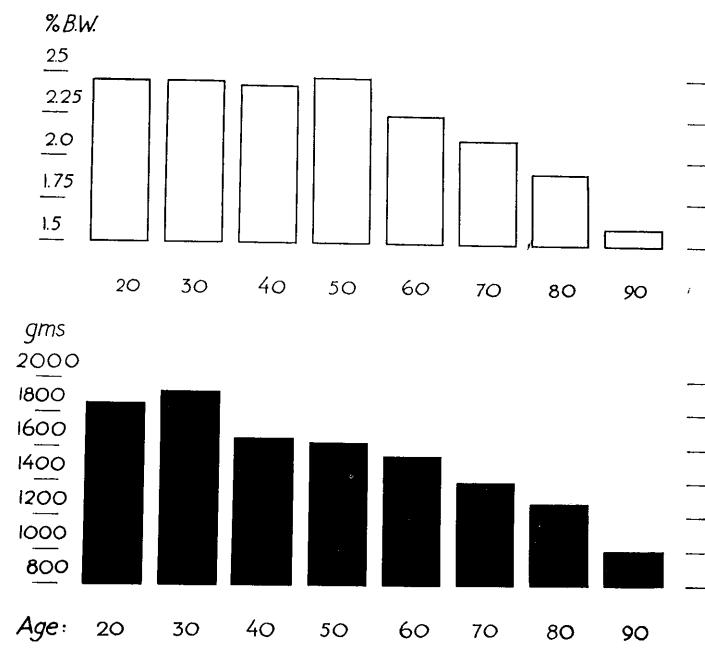


FIG. 3. Changes in liver weight with aging. Absolute weight, black columns; percentage of body weight, white columns.

ging. Left ventricle, black

with uniform progression. However, when these values were changed to percentages of body weight, a different picture appeared. The liver retained its percentage relationship to body weight until about age 50, and thereafter it became relatively smaller (7). Immediately the old problem raises its head again. Did the liver actually become smaller? Was the liver unable to increase in size with age—that is, as time passed was there no need for the liver to increase with age? Or did those people who died by the time they were 50 do things to their livers that caused them to enlarge, and at the same time caused a shortening of their lives?

One would suspect from other data that the liver becomes a smaller and smaller part of the body as time goes on but, as has been shown in the preceding paper (1), to make our observations complete it is necessary to know statistically what happens for the group from birth to death. It is indeed difficult, if not impossible, to make observations on the liver of any particular person and interpret them from the standpoint of geriatrics or senescence. Unpublished studies (8) on the kinetics of liver function with age indicate that the liver retains the capacity to function at an undiminished rate as time passes.

With regard to heart size (Fig. 4), again we note a similar process in the enlargement of the heart with time. It would seem, however, that in terms of percentage of body weight, the heart increased in size to age 70 and thereafter tended to become smaller. This interpretation, obviously, is open to serious question. Again, we cannot answer the questions: Did those persons who lived to be 80 or 90 have hearts that were resistant to enlargement? Did they have outflow tracts that did not cause the heart to enlarge? Or did the hearts become smaller with time, in response to decreased demands?

Figure 5 shows the same type of difficulty in interpreting the changes in the spleen. It would seem that the spleen actually became smaller. This may be true, but we cannot say it with certainty since the persons who survived either

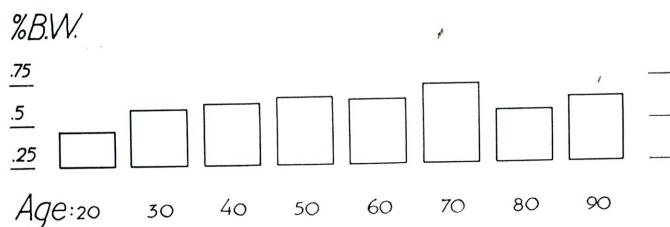


FIG. 4. Changes in heart weight (percentage of body weight) with aging.

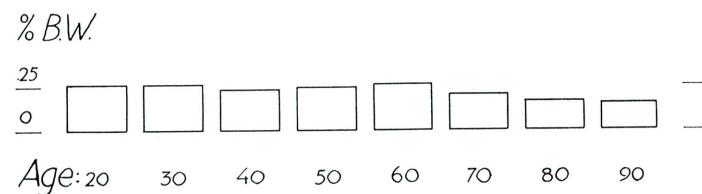


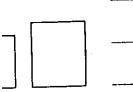
FIG. 5. Changes in spleen weight (percentage of body weight) with aging.

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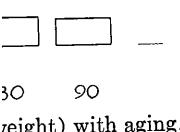
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may have had small spleens that were never affected by anything causing enlargement, or they may have had spleens capable of becoming smaller with the passage of time.

#### DISCUSSION

The data presented here on 400 autopsies illustrate the difficulties inherent in the proper interpretation of the events that cause changes in organ size. According to these data, the liver, heart and spleen would be smaller at age 80 than at age 30; the adrenals and kidneys would also be smaller and the lungs would be larger. Respective situations would hold for all the organs we were able to measure.

When it comes to the interpretation of these findings, however, some previously noted uncertainties in geriatric data become apparent. There are no firm answers to such questions as: Were the persons who lived to advanced age those whose lungs were capable of increasing in size? Or was there a gradual accumulation of fluid in the lungs as these persons became older? Or did the lung changes occur in response to changes in the skeletal structure and thus represented only passive enlargement? Some questions that can be raised do not seem cogent, yet we do not have answers. As the individual becomes more inefficient with time, is it necessary for him to have more air, or to have a larger lung surface to absorb the air? Is this the reason for enlargement of the lungs? These questions point out our inability to interpret accurately much of the data we accumulate (9).

#### CONCLUSIONS

Geriatrics is a field in which accurate interpretation is needed—not only accurate interpretation, but precise measurement of all of the processes that at present fail or *can* fail to provide information regarding qualitative and quantitative differences in persons who do not survive.

An examination of death curves will show that what is seen at autopsy in the so-called senescent patient is simply an observable variation between individuals. Since there is a relationship between time and death rates that starts very early in life—perhaps at age 3 or 4, if not earlier—then there must be unmeasurable factors which alter the length of time one person will survive compared with another. These factors cannot be all environmental and neither can they be all inherent, but are an interplay of the two. Thus, to attempt to interpret autopsy material purely on the basis of the findings in one or several subjects is to separate these observations from the continuous spectrum of stresses and responses that the person has lived through.

Data of the type presented here on 400 autopsies are of general value, but the ultimate explanation of the factors influencing survival or death with aging is not to be found in either gross or microscopic tissue examination. The answer lies in an exact knowledge of the several thousand reactions which occur in the cell continuously. This is the gigantic uncertainty that faces the geriatric research worker.

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