laboratory, is derived from a line which traces back to a generation above the points at which these changes occurred. Both of these non-cancerous families have been lost unless some one of the workers to whom Mr. Marsh sent mice, between 1930 and 1935, has continued the inbred line.

With two exceptions, we do not know to whom Mr. Marsh sent mice. We should be very glad to have such persons correspond with us.

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SPECIAL ARTICLES

CHANGES IN HUMAN TISSUE ELECTROLYTES IN SENESCENCE[1]

THERE are many reports of chemical alterations as animals increase in age up to maturity, but there have been few studies in which senescent animals have been compared with younger mature animals. We consider an animal to be senescent when it has lived three fourths of its maximum life span (taking one hundred years as the life span of humans) and that the younger mature animals used for comparison should be at least twice the age of sexual maturity.

For the analyses of human tissues which are reported in this paper two principal age groups were selected. The senescent group was seventy years old, or over, with an average of seventy-five years. The younger group, which served as a standard for comparison, consisted of individuals from thirty to forty years old, with an average of thirty-five years.

Tissues were obtained from autopsies, some from accident cases and others from pathological cases. These will be discussed separately. The accident cases[2] were people who appeared to have been in good health until killed suddenly by automobiles, by falling or by murder. Only those cases were analyzed where there had been a quick death uncomplicated by poisoning or intoxication. The analyses of eleven accident cases between the ages of thirty to forty years, with an average of thirty-five years, were taken as a standard for comparison with senescent tissues.

Table I represents the changes found in senescence. Tissues from six accident cases over seventy years old, having a mean age of seventy-five, were analyzed. Each value in Table I is the per cent. deviation from the standard values for younger tissues. It will be noted that, except for the heart water, there was an increase in water, chloride, total base, sodium and calcium. Furthermore, there was a decrease in potassium, magnesium, phosphorus, nitrogen and ash in all the tissues except the liver.[3]

TABLE I

PER CENT. DIFFERENCES IN ANALYSES OF HUMAN TISSUES FROM ACCIDENT CASES OVER SEVENTY YEARS OLD RELATIVE TO TISSUES FROM ACCIDENT CASES THIRTY TO FORTY YEARS OLD

Constituent	Kidney	Liver	Spleen	Psoas muscle	Heart	Average of tissues	
H_2O	+ 2.6	+ 1.7	+ 2.8	+ 0.8	- 1.4	+ 2.	XH
Cl*	+(2)	+(18)	+(12)	+(56)	+(25)	+(23)	
Total Base.	+ 3.	+ 12.	+ 4.	+ 6.	+ 7.	+ 7.	
Na	+ 5.	+ 15.	+ 21.	+ 62.	+ 0.3	+ 20.	
Ca	+60.	+ 4.	+ 14.	+ 33.	+ 31.	+ 28.	
K	-19.	+ 6.	- 13.	- 7.	- 9.	- 12.	XL
Mg	- 9.	+ 17.	- 10.	- 11.	- 2.5	- 8.	XL
P	-13.	- 0.1	- 8.	- 12.	- 2.	- 9.	XL
N	- 9.	+ 8.5	- 13.	- 3.	- 4.	- 7.	XL
Ash	-11.	+ 1.	- 8.	- 1.	0.	- 5.	XL

* The chloride values are less accurate than the other values in this table.
XH signifies that the average for the tissues does not include the heart.
XL signifies that the average for the tissues does not include the liver.

These changes in senescence were corroborated by our data on pathological cases obtained from autopsies in this department. Tissues from people over seventy years old were compared with tissues from people between thirty to forty years, all of whom died of disease. Eighty per cent. of the changes were in the same direction as those found with accident cases (Table I). These tissues were from patients who had died from the following diseases: carcinoma, nephritis, leuetic aortitis, brain abscess, arteriosclerosis and partial ileus. Pneumonia was a complication in three cases. Cases with severe infections or marked wasting were not taken and pathological organs were avoided as far as possible.

Partial further corroboration of the senescent changes was obtained by comparing another group of five pathological cases which were from sixty-five to seventy years old, with the young pathological cases. At this age only part of the changes were found, namely, those of total base, calcium, phosphorus and ash, with a moderate increase of chloride. On the other hand, these sixty-five to seventy year cases did not show significant changes of water, sodium, potassium, magnesium or nitrogen.

We do not consider these differences between old and young pathological tissues as being significant, except in so far as they substantiate the changes in old

1 This investigation has been aided by a grant from the Josiah Macy, Jr., Foundation.

2 The tissues from accident cases were obtained with the cooperation of Dr. Milton Helpern and other members of the Medical Examiner's Office of New York City.

3 The values in Table I are calculated on a wet weight basis. When converted to a dry weight basis the positive values became even more significant, while the negative values became less significant. The nitrogen and ash did not decrease on a dry weight basis.

age found by the analyses of tissues from accident cases (Table I). In order to determine the effect of disease on the tissues the young pathological and accident cases were compared. Except for calcium, which was lower in the pathological tissues, there was a tendency toward changes in disease similar to those found in senescence. The magnitude of the changes in disease was less than in senescence, except in the case of magnesium. The present data do not warrant further comparisons. Extensive studies of tissue changes in selected diseases should be instructive. However, it is necessary to determine whether the differences found in tissues from patients dying of disease were produced progressivly with the advancement of the pathological condition or whether they arose in the terminal state preceding death.

These preliminary results are presented with no attempt to interpret their significance. Detailed analyses will be published after more data have been obtained. Only minor modifications of the average values for accident cases are to be expected as more tissues are analyzed. On the other hand, we do not claim that the analyses of pathological tissues are representative, but we feel that further work in that field would be profitable.

SUMMARY

Analyses of tissues from people over seventy years old who died from accidents were compared with analyses of tissues from thirty to forty-year-old people who also died from accidents. The old tissues contained more water, chloride, total base, sodium and calcium; and they contained less potassium, magnesium, phosphorus, nitrogen and ash than the younger tissue.

Tissues from pathological cases of the same two age groups showed the same changes after seventy years. Only part of these changes were found in tissues sixty-five to seventy years old.

Tissues from young pathological cases when compared with accident cases of the same age were found to have undergone changes similar to those found in senescence, but to a lesser degree. Calcium formed an exception.

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EFFECTS OF CARBOHYDRATE PLETHORA IN EXPERIMENTAL DIABETES

IN a recent study of carbohydrate metabolism[1] it was concluded that the depancreatized dog in the early stages of fasting was unable to oxidize administered glucose, since there was no fulfilment of the necessary criteria, *i.e.*, an elevation in respiratory quotient, a corresponding diminution in the amount of extra glucose excreted, a protein-sparing action and a ketolytic effect. Since the completion of that work Mirsky and co-workers reported that ketolytic[2] and nitrogen-sparing[3] effects were produced by injection of large amounts of glucose into depancreatized animals. The quantities administered were such as to lead one to expect glycogen formation, even in the absence of insulin,[4] although no data were reported on this point. Because of the suggestion that the deposition of glycogen in the depancreatized animal may result in oxidation of this material, we are reporting experiments on nephrectomized-depancreatized dogs conducted without anesthesia in order that respiratory metabolism, as well as blood constituents, could be studied.

Of nine operated animals, only three satisfactory preparations were obtained. In these, one kidney was removed and, ten days later, a loose tie was placed around the blood vessels of the remaining kidney at the time of pancreatectomy. Food and insulin[5] were administered to the animals until four days before the following experiment was conducted. A blood sample was drawn, functional nephrectomy was performed by tightening the kidney tie, and a basal metabolism period obtained for three to four hours. At the times noted in Table I blood was drawn and glucose injected

TABLE I

EFFECTS OF GLUCOSE INJECTED INTO NEPHRECTOMIZED-DEPANCREATIZED DOG

Time after nephrectomy	Glucose injected	R.Q.	Blood constituents				Air Acetone
			Sugar	Acetone bodies	Non-protein N	Lactic acid	
hr.	gm.		mg. per cent.				mg./hr.
0	0		345	43	38	22	
4	0	0.73	430	49	55	25	51
11	25	0.72	1250	41	71	32	36
16.5	25	0.74	1727	33	83	38	23
21.5	25	0.74	2000	19	91	42	18
26	0	0.74	2022	10	94	45	13

intravenously. In the intervening time the animal was replaced in the chamber for determinations of the respiratory metabolism. Table I summarizes the data obtained on a single, representative animal. The absence of any significant change in the respiratory

[1] S. B. Barker, W. H. Chambers and M. Dann, *Jour. Biol. Chem.*, 118: 177, 1937.

[2] I. A. Mirsky, J. D. Heiman and R. H. Broh-Kahn, *Amer. Jour. Physiol.*, 118: 290, 1937.

[3] I. A. Mirsky, J. D. Heiman and S. Swadesh, *Amer. Jour. Physiol.*, 119: 376, 1937.

[4] S. G. Major and F. C. Mann, *Amer. Jour. Physiol.*, 102: 409, 1932.

[5] We wish to express our appreciation of the generous amounts of insulin supplied by the Eli Lilly Company.