It may be well to point out that in Jordan's[2] study of the epidemiology of influenza, the conclusion was reached that any connection between these two diseases was probably fortuitous.

It is well recognized that, except in times of epidemic, the diagnosis of influenza is often loosely made. Since the discovery of the virus of influenza, it has been possible to make the diagnosis with a high degree of accuracy by the study of the neutralizing power of the serum after convalescence.

During the past several months, a certain number of cases have come to our attention in which an acute respiratory infection diagnosed as grippe or influenza has been followed within a short time by the development of various neurological conditions. In sixteen such instances the serum of the patients has been obtained within one to three or four months after the upper respiratory infection. These serums have been tested for influenzal antibodies according to the procedure of Francis and Magill.[3] In fourteen instances no protective antibodies were demonstrated in the serums. In one instance, the serum virus mixtures indicated slight protection and in one instance, a partial protection. In no instance was there complete protection. It, therefore, seems reasonable to assume that the original diagnosis of influenza or grippe had been incorrect in at least fifteen of the cases.

Further indications that the virus of influenza is not an etiological factor in cases of encephalitis or encephalo-myelitis is afforded by two facts: first, in a personal communication Francis has stated that in experimental animals the virus of influenza does not invade the central nervous system; second, Dr. L. S. Snegireff, of the New Jersey State Health Department, has given me permission to quote him to the effect that in investigating several New Jersey state institutions, where epidemics of influenza have occurred, there has been no instance in which encephalitis has developed during or following the outbreaks of influenza.

These data indicate that there is no etiological relationship between encephalitis and influenza. It is obvious that further work must be done to confirm or refute this opinion.

Two questions arise which await further investigation. When encephalitis or encephalo-myelitis follows an upper respiratory infection (diagnosed as grippe or influenza), are these early symptoms the first stage of the central nervous system infection or does an upper respiratory infection (not influenza) lower the barriers of resistance of the naso-pharyngeal mucosa to a virus either latent or acquired? This latter question presupposes that the virus or viruses of encephalitis may gain entrance through the naso-pharyngeal mucous membrane. On this point there is no definite information. However, it is quite generally believed that this is the portal of entry of the virus of poliomyelitis and of the St. Louis type of encephalitis.

We hope that this brief report will lead to further investigations by others, and we trust that we shall have the opportunity to carry on more work.

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[2] E. O. Jordan, "Epidemic Influenza," 1927; published by the American Medical Assn.

[3] Francis and Magill, *Jour. Exp. Med.*, 63: 5, 655–668, May 1, 1936.

THE OCCURRENCE OF A POSSIBLE MUTATION, CANCER TO NON-CANCER, IN THE HOUSE MOUSE

THE late Millard C. Marsh, in an attempt to demonstrate his theory that the irritation caused by intestinal nematodes (*Aspiculuris tetraptera*) was directly responsible for the appearance of mammary tumors in mice, developed a large colony of these animals in which the incidence of breast tumor was unusually high (80 to 100 per cent.). In support of his theory, he cited the behavior of these tumors when the experimental colony was freed from the parasites. In these mice he noticed that the tumor incidence was gradually becoming less and less.

Due to the fact that other workers, to whom he sent breeding stocks, of this strain, were unable to obtain the high tumor incidence recorded by Marsh an attempt has recently been made to determine the true incidence of cancer of the breast, in his stock.

In tabulating Marsh's data, it was noticed that this decline in cancer incidence among females of the worm-free colony was largely due to the inclusion, in the strain, of two families none of the members of which developed tumor. Tracing back the pedigrees of the first of these families, it was found that a mouse in his generation "Y," which itself had a mammary tumor and the female ancestors of which for 18 generations back had all been cancerous, gave rise to a line none of the members of which developed tumor. This line extended through twelve generations and contained 112 mice.

The female which gave rise to the second non-cancerous family was cancerous herself and had an ancestry of eight generations of tumor. All her descendants, which extended through eight generations and which numbered 28 females, were non-tumorous.

When these 140 animals are deducted from the data making up the incidence curve for the worm-free stock, the percentage of tumor remains remarkably constant in its range, for the different age periods (between 80 and 85 per cent.).

Unfortunately the stock, as it now exists in this

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.