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VISCERAL ORGANISMS *

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In previous articles¹ it was shown that connective tissue could be kept *in vitro* for several months in a condition of active life, and that a fragment of heart could pulsate normally for more than one hundred days after its extirpation from the animal; but the quantity of connective tissue maintained in permanent life was very small. It would be important, for the study of many problems, to keep entire organs alive outside of the organism. Therefore I attempted to develop a technic by which a system of organs could be caused to live *in vitro*.

The method consisted of removing aseptically, *en masse*, heart, lungs, liver, stomach and part of the intestines, pancreas, adrenals, kidneys and spleen of an animal, a cat generally being used, and preserving these organs in an incubator at the temperature of 38 C. (100.4 F.), while the lungs were being artificially ventilated.

The operation comprised five stages:

1. A cat was etherized. The skin of the anterior part of the neck, thorax and abdomen was sterilized. Then the esophagus was ligated and severed under aseptic technic. The trachea was cut transversely and a glass tube inserted in its lumen. A catheter was introduced into it as far as the bifurcation, according to the Meltzer and Auer method.

2. The abdomen was opened. The aorta and vena cava were tied and cut in the lower part of the abdomen. The small intestine was cut under aseptic technic. The ureters were severed. Then the aorta and vena cava were isolated from the posterior walls of the abdomen and their posterior branches tied. The peritoneum surrounding the kidney was dissected. The splanchnic nerves were cut. Then the abdominal viscera were wrapped in a Japanese silk towel, thus being completely separated from the abdominal wall. They remained united to the animal by the aorta and vena cava.

3. The thoracic cavity was opened and the mammary vessels were clamped. Then the thorax was severed longitudinally, and the diaphragm completely separated from the thoracic wall. Artificial respiration was established. The anonymous arteries were tied, and the animal died. The superior vena cava and the azygos vein were tied and cut. The vagus, sympathetic and phrenic nerves were severed. All the posterior branches of the thoracic

aorta were cut. Generally the heart pulsated weakly and the blood-pressure was very low.

4. Then the thoracic and abdominal viscera, united through their blood-vessels, were removed from the cadaver of the animal, and placed in a tray containing Ringer's solution, at about 38 C. Ordinarily the heart still pulsated slowly and regularly. But the blood-pressure was very low, the arterial pulsations weak and the appearance of the organs very anemic. A careful hemostasis of the small vessels was made. After a few minutes the blood-pressure rose and, in a few cases, became almost normal. Generally a blood transfusion was made from the carotid artery of another cat to the inferior vena cava of the visceral organism. Then the lungs became pink, the blood-pressure was higher than normal and the heart was beating strongly from 120 to 150 per minute. The abdominal aorta pulsated violently, and strong pulsations could be seen in the arteries of the stomach, liver and kidneys. Peristaltic contractions of the stomach and of the intestines were observed. If, a few minutes after the transfusion, the pressure was still above normal, a quantity of blood was allowed to flow from the lower part of the abdominal aorta. Then, the appearance of the viscera was the same as the viscera of a normal animal.

5. The visceral organism was placed in a tin box filled with Ringer's solution, covered with thin Japanese silk and protected by a glass cover. The tracheal tube and the esophageal tubes were fastened to proper openings in the anterior wall of the box. Artificial respiration was carried on by a continuous current of air interrupted ten times per minute. Dr. Meltzer kindly examined the respiratory conditions in these experiments, showing me a method for obtaining a proper ventilation of the lungs. He has contributed, in a large measure, to the rapid success of these experiments. Water or food could be injected into the stomach through the esophageal tube. The intestine was pulled through a glass and rubber tube fixed through the posterior wall of the box. The end of the intestine was fixed by a circular suture to the edge of the rubber tube, an artificial anus being made. The box was then put into an incubator at a constant temperature of about 38 C.

It was then observed that the viscera were living in an apparently normal condition. The pulsations of the heart and the circulation of the organs were normal. The intestine emptied itself through the artificial anus by regular peristaltic contractions. When the intestine was empty, bile and intestinal juices were evacuated. In an experiment in which the stomach was full of meat at the time of death, normal digestion occurred. After five or six hours, hyperemia of the peritoneum of the intestine appeared. It seemed as though peritonitis developed progressively and in some cases the intestine was paralyzed. Nevertheless, the circulation remained

* From the Laboratories of the Rockefeller Institute for Medical Research.

1. Carrel, Alexis: *Rejuvenation of Cultures of Tissues*, THE JOURNAL A. M. A., Nov. 11, 1911, p. 1611; *Jour. Exper. Med.*, 1912, xv, 516. Pozzi, C. R.: *Bull. de l'Acad. de méd., Paris*, June, 1912.

excellent and a section of a small mesenteric artery produced an abundant hemorrhage.

Some of the visceral organisms died almost suddenly after three or four hours, but most of them were still in normal condition ten hours and even twelve and thirteen hours after the death of the animal to which the organs belonged. The death of the visceral organism was announced by some irregularities in the pulsations of the heart, which were also weaker. Then the heart stopped suddenly.

In the last experiment the death of the visceral organism occurred thirteen hours and fifteen minutes after the death of the cat from which it originated. It is probable that the duration of life will be increased by certain modifications of the technic; but, as it is, a visceral organism can profitably be used for the study of many physiologic and chemical problems.

Sixty-Sixth Street and Avenue A.

A STUDY OF THE CAUSES OF DEATH IN
ONE HUNDRED PATIENTS WITH HIGH
BLOOD-PRESSURE*

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In a study of the subsequent histories of some 500 persons showing a systolic blood-pressure of 170 or over, seen in my consulting practice or in that of my father during the past eight years, it was found that approximately 150 patients were known to have died. For 100 of these, accurate information as to the date of death, the exact cause of death, and the important later symptoms was obtained. The latter data I owe largely to the prompt and cordial cooperation of the family physicians of these patients in answering my somewhat numerous inquiries, and I desire here to express my appreciation of their assistance. A study of this character, of an essentially chronic group of diseases, is possible only in private practice, among patients of the intelligent classes; it is impossible with any hospital material, however large. Many of the problems regarding the causation and development of the so-called degenerative diseases of later life are to-day a fruitful field for truly scientific investigation by the general practitioner.

From the very nature of the investigation, the exact determination of the primary disease underlying the state of high arterial pressure in each case is impossible, and the clinical diagnosis must be a matter of personal opinion based on a consideration of all the symptoms and signs during life. An ideal study would include a complete autopsy of each case; but for the purposes I had in view, 100 cases of hypertension followed from the first symptom to death, with notes of my personal observations, are of more value than a like number of hospital autopsies. My personal impression, gained in part from such a hospital experience of a one-sided kind, the patients being of the lowest social class, has always been that the most frequent mode of death in chronic nephritis is by gradual cardiac insufficiency. My desire to obtain exact information on this point among the well-to-do, and further to determine, if possible, whether the initial symptom or the prominent early symptoms associated with high blood-pressure are indicative of the prob-

able death to be expected and, therefore, to be guarded against, was my motive in undertaking the analysis. It is clear from the character of the material studied that the less chronic and more progressive types of nephritis associated with marked general edema will be inconspicuous as contrasted with their frequency in a hospital service.

CLASSIFICATION BY CLINICAL DIAGNOSES

My clinical diagnoses of the primary underlying diseases of 100 patients were as follows:

Chronic nephritis (no attempt to differentiate anatomic types)	79
Diabetes	7
General arteriosclerosis	4
Coronary sclerosis	4
Aortic regurgitation (possibly syphilitic aortitis)	2
Aortic aneurysm (probable)	1
Primary myocardial disease	1
Paroxysmal tachycardia (with secondary myocardial insufficiency)	1
Hypertension without nephritis, evident arteriosclerosis, or cardiac disease	1
Total	100

In all the cases of diabetes, chronic nephritis or some manifestation of arterial disease had supervened on a preexisting diabetes. This, of course, is common; and the figure is almost identical with my statistics of four deaths from chronic nephritis among fifty fatal cases of diabetes observed within the same period. Out of 220 diabetics, again, fifty showed high blood-pressure—another evidence of the frequent association of cardiovascular and renal disease with diabetes in elderly individuals. In the younger patients with pure diabetes, terminating so frequently in coma, high blood-pressure is not observed; diabetes, therefore, stands in no direct causal relation to the high blood-pressure, but in individuals past middle life it seems to predispose to the development of those changes which produce hypertension. Elliott has reported similar findings, which contradict the idea of Potain that diabetes is a hypertensive disease.

In the entire series, pericarditis was definitely diagnosed once and suspected only one other time. Since pericarditis is found at autopsy in such patients distinctly more frequently than this it is highly probable that it was overlooked. Of the four cases of arteriosclerosis without proof of nephritis, in one there was a pressure of 170, and in the other three it was over 200. It is possible that these patients had contracted kidneys, for as a rule general arteriosclerosis is unassociated with increased blood-pressure. On the other hand, many of the younger individuals in this group with evidences of severe chronic nephritis showed the most extensive and extreme peripheral arteriosclerosis. Of the five patients below 40 years of age, however, only two men, respectively 32 and 36 years old, had arterial thickening; but in them it was extreme. In the non-fatal cases of the larger group of 500 are a number of patients in whom high blood-pressure and associated cardiac hypertrophy are the only objective evidences of disease. The latter are largely women. The single similar case in this series of deaths was a woman, aged 74, who had had high blood-pressure for six years, associated only with neuralgic pains and mental depression. Her pressure ranged between 190 and 200. She died of pneumonia, having developed some symptoms of failing heart during the months preceding her death.

* Read in the Section on Practice of Medicine of the American Medical Association, at the Sixty-Third Annual Session, held at Atlantic City, June, 1912.