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THE FACTORS OF SAFETY IN ANIMAL STRUCTURE AND ANIMAL ECONOMY*

S. J. MELTZER, M.D.

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THE living animal body is like a machine in action. Like a machine, its structures are subjected to a variety of stresses and, like a machine, the work is accomplished by an expenditure of energy derived from a supply of fuel. I intend to discuss in this lecture whether, as in the human made machines, the structures and functions of the animal mechanism are provided with factors of safety. The term "factor of safety" is employed in engineering to designate the margin of safety required in the building of engines, bridges, houses, etc. For instance, in designing a boiler, if the tensile strength of the steel of which the plates and stay-bolts are made is 60,000 pounds per square inch, the actual stress which is allowed for the work of the boiler should not be more than 10,000 pounds per square inch for the plate and not more than 6,000 pounds per square inch for the stay-bolts; that means the stress to which the plates or the bolts may be exposed in the boiler should only be one-sixth or one-tenth of the actual strength of the steel. The factors of safety are said to be here six for the plate and ten for the bolts. In some instances the required factors of safety may be as low as three, in other cases again they may be as high as twenty and even forty. The character of the stress to which the structures might be subjected is an important point in deciding on the size of the margins of safety. Structures, for instance, which are to be employed for alternating loads require high factors of safety; the highest margin of safety is required when the structures

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are subjected to rhythmic shocks. In constructing a bridge or a machine, it is then calculated that the structures should be capable of withstanding not only the stresses of reasonably expected maximum loads, but also the stresses of six or ten times the size of such loads. The factor of safety has its foundation in our ignorance of what might happen and in the reasonable desire to meet unexpected contingencies. Some writers are, therefore, inclined to designate the factors of safety as factors of ignorance.

It is obvious that the factors of safety are applicable not only to the structures, but also to the supply and expenditure of energy of the machine. The supply of fuel is calculated to have the engine in readiness not only for expected maximum work, but also to be capable of meeting unexpected contingencies. On the other hand, when there is no exceptional need for it, no engine is allowed to perform maximum work; this economy here is again a factor of safety.

Are the structures and the functions of the living animal body provided with such factors of safety? As far as I know, that question has never yet been clearly raised, and certainly was never made the subject of a direct investigation. There is, however, no lack of casual remarks bearing on that problem and these are manifestly unfavorable to an assumption of the existence or requirement of factors of safety in animal organisms. On the contrary, there are many to whom it is apparently self-evident that Nature is economical and wastes neither material nor energy. Theories and practical suggestions are based on such a view as a premise which seems to their authors to require no special proof. Verworn, for instance, asserts that the assumption of special inhibitory nerves for skeletal muscles can be rejected, *a priori*, because the presence of such nerves would be a waste of matter and energy and in contradiction with the prevailing principle of economy in the animal body. Another instance is the extreme position held by some recent writers with respect to the supply of energy to the animal machine. Factors of safety, maximum or optimum supply of

fuel, do not come in for a consideration in the discussion of these writers.

A MINIMUM DIET THE IDEAL STANDARD OF DIET.

The argument is directed against the use of a dietary standard which represents the average mean supply of energy, the minimum supply of food being considered as the ideal standard of diet. As is known to all, Professor Chittenden and his co-laborers have carried out nutrition experiments of long duration on a number of men. The essential feature of these experiments was the use of a low proteid diet; in some instances the diet was also combined with a considerable reduction in the caloric values of the food. All the subjects of the experiments retained their usual health. Professor Chittenden admits that the diet used in these experiments, especially with regard to the proteid intake, represents the minimum requirement of the human body; he nevertheless earnestly advocates its acceptance as a general standard of diet, assuming *a priori* that the minimum food with which a number of men can manage to live for some time without harm, is the desirable standard of supply of energy for all animal machines. Whereas, in the economy of the human-made mechanisms, and, in fact, in the economies of all human organizations, decrease in supplies and increase in expenditure leads invariably to disaster, it would seem that in the physiologic economy of the living mechanism such a procedure may even lead to a greater efficiency of the mechanism. Professor Irving Fisher tells us recently that nine Yale students, under the influence of prolonged mastication of a diet greatly reduced in proteid and in caloric values, gained very much in endurance in performing certain physical tests.

Is there, indeed, a difference between the economies of human-made organizations and those of the living organism? I have stated above that the factors of safety in mechanical constructions are, after all, only factors of ignorance. Possibly wise Nature constructs her organisms on such an efficient principle

which permits the accomplishment of the greatest amount of work on a minimum supply of material and energy. It would be a fascinating distinction between a dead mechanism and a living organism, if true.

SAFETY AND ECONOMY IN THE ORGANISM.

The subject of this lecture will be an investigation of this question, an investigation whether the structures and functions of the animal organism are constructed with a special consideration for the greatest economy or for the greatest safety. Or, to leave the purposefulness of the organization out of discussion, I may, perhaps, put it more correctly by saying that it will be essentially an investigation into the ratios of the supply of material in many organs of the body to the amount of work they are expected to perform. I believe that the investigation may lead to some instructive general conclusions of a theoretical and practical character. As already stated, the problem seems to me to be new and, as far as I know, no original investigations were carried out with the special purpose of solving it. There are, however, a great many well-established facts brought out in theoretical and practical work undertaken for other purposes, which are, nevertheless, capable of throwing a good deal of light on our problem. Such facts have the advantage of being unbiased witnesses, since no preconceived theory was at the bottom of their discovery. My task will consist in reviewing these facts as far as they are available, or more correctly, as far as they are known to me, and bringing them impartially in proper relation to our problem.

FACTORS OF SAFETY IN THE PLAIN TISSUES.

I shall commence with the plain tissues of the body. In the multitude of studies on these tissues there are not many investigations which could be utilized for our purpose. However, a series of careful investigations, recently published by Triepel, have an intimate bearing on our problem. Triepel investigated the elasticity and resistance of several tissues, like muscle, ten-

don, elastic tissue, bone, cartilage, etc. For us the following statements are of special interest. For muscle, tendon and elastic tissue, Triepel found that the maximum stretching which may occur in the animal body is not far below that degree which can cause tearing of these tissues. The resistance of bones and cartilages to a crushing stress is, however, far above any stress which might occur in normal life. With regard to muscle, tendon and elastic tissue it appears therefore that the structures in themselves have practically no factors of safety above the maximum stress to which they might be subjected. Any unexpected tension above the maximum occurring in ordinary life might lead to a rupture of these tissues. Triepel, however, calls attention to the fact that the degree of stretching of these tissues is greatly limited by their connections with the structures surrounding them, especially by the skeletal parts. These limitations will, for the most part, prevent these tissues from reaching their breaking point. We may then say that muscle, tendon and elastic tissues have no factors of safety in the structures themselves; but they are provided nevertheless with some such factors by their connections with other tissues. The bones and cartilages, on the other hand, which are but little influenced by other tissues, are provided with a very large margin of safety over the stresses to which they might normally be exposed. Triepel here makes a remark which has a direct bearing on the problem with which we are dealing. He says that the large surplus of material in bone and cartilage tissue shows that Nature does not follow the law of obtaining a result by the smallest possible means.

It is worth noticing that the large margin provided here cannot have the object of offering protection against unexpected contingencies coming from within the body, as these, according to Triepel, will never reach even the yield point of these tissues. The protection is here provided against contingencies coming from without, against injuries of external origin. It is a protection not against an internal, a physiologic calamity, but against an external, so to say, pathologic contingency.

SAFETY FACTORS IN THE MORE COMPLEX TISSUES.

A sufficient number of readily available data for the study of our problem we find in researches on complex tissues or organs. We shall begin with the bilateral mechanisms. Here are, in the first place, the kidneys. Every medical man now knows that one kidney can be removed with entire impunity if the other kidney is normal. The amount and the composition of the urinary secretion remains practically unaltered, and this even soon after the removal of the kidney. That can only mean that normally the kidney has an abundance of tissue which can do, at a moment's notice, at least twice the normal amount of work. From the experimental work of Tuffier, Bradford and others we know that at least two-thirds of both kidneys may be removed without serious detriment to the animal's life or to the secretory function of the kidneys. At the same time, we must remember that the normal secretion represents by no means the minimum amount of work of the kidney. We know that the average quantity of the urine, as well as the normal quantities of its various constituents, may be greatly reduced without any visible detriment. In fact, there may be anuria for many days without any serious symptoms, and perhaps also without serious consequences, if the anuria be not due to a disease of the kidney, but to such causes as hysteria, calculus, reflex or compression. The margin of safety in the tissue of this eliminating organ amounts, at least, to twice its normal need.

This would seem to be an unreasonable luxury, a waste. But what a blessing. For a score of years, or more, in many of us the kidney is gradually losing some of its valuable material from one cause or another without any symptom, without a reminder sufficient to spoil our pleasure of life or to hamper our activities. Not until that luxurious surplus is approaching its exhaustion do we get a warning. But then our work is mostly done and our time limit nearly reached.

Next we shall consider the lungs, an organ of supply and elimination of first order. We all know that life may continue

though a great part of the lungs be destroyed, if only the disease which caused the destruction comes to a standstill. We know that in some cases of pneumonia one lung can be entirely consolidated without seriously impairing the process of ventilation. Furthermore, a patient whose thorax was freely opened to evacuate a one-sided pleural abscess has, after the opening, less dyspnea than before. In empyema, as in pneumonia, it is essentially the infection and intoxication with their reactions which cause the apparent disturbance in the respiratory mechanism, and not so much the mechanical interference with the ventilation of the corresponding lung. Since the classic experiments of Regnault and Reiset, many investigators have stated that compression of one lung, or a unilateral pneumothorax, exerts very little influence on the respiratory exchange of gases. Hellin reported, recently, a series of experiments on rabbits in which the right lung was completely removed. The right lung of the rabbit has four lobes and is much larger in volume than the left; that means that more than one-half of the lung tissue was removed. Most of the animals survived the operation and some lived a year and longer. Except for a temporary moderate dyspnea, lasting only an hour or two, the animals were in a normal condition, and the respiratory quotient continued to be, after the removal of the lung, exactly as it was just before the operation. We see, then, that the normal process of respiration can be carried out with at least one-half of the lung tissue and probably with a good deal less. We have here, with regard to the quantity of tissue, a factor of safety equal at least to two, which does not appear to be an excessive margin considering the importance of the function which that tissue has to carry out.

Of the bilateral organs of reproduction, we know from numerous surgical operations that the removal of one ovary or of one testicle does not interfere in the slightest degree with the corresponding functions of the individual. For the female organs it has been frequently established that even a small part of one ovary is sufficient to carry on the function

of menstruation and conception. In fact, there are a number of reliable cases on record in which pregnancy occurred after the removal of both ovaries, which cases were explained by the assumption that some particle of normal ovarian substance was caught in the ligature and retained in the body, and this fragment was then sufficient to carry out the function of ovulation and conception.

For the testicles we may safely assume also that a small fragment of one testicle left in the body would be capable of carrying on the function of reproduction. But I have not come across experimental or surgical data which directly bear out this assumption. There are definite data with regard to the secondary sexual characteristics in fowls. If in the process of castration some fragment of one testicle is left, the cock, according to Foges and others, does not lose the comb and other secondary sexual characteristics. However, these secondary characteristics are probably connected with the internal secretion of these organs, and their persistence might not be a sufficient proof for the persistence of the function of reproduction. At any rate, it is sufficiently evident, especially as will be seen later, that the tissues of the organs of reproduction are greatly in excess of the maximum need of the chief function of these organs.

Among the bilateral organs there are two whose functions are carried on exclusively by internal secretion. I mean the thyroid and the adrenal glands. We do not notice their activity while they are present, but we recognize their importance by the serious effects which follow their removal. The complete removal of both thyroid glands is followed either by acute symptoms of a tetanic type or by chronic states which are known under the names of myxedema and cretinism. It is, however, a well-established fact that the removal of four-fifths or even five-sixths of both thyroids is not followed by perceptible consequences, which means that one-fifth or one-sixth of the entire gland is sufficient to provide the body with the indispensable substance contained in the secretion of the gland. It was just on that account that, at first, the experimental

results showing the importance of this gland were disputed by some observers; small accessory glands were hidden in some cases which made the apparently complete removal of both thyroids ineffective. The thyroid gland possesses accordingly four or five times more tissue than is necessary for the complete maintenance of health and life of the animal.

In recent years some of the symptoms following the removal of the thyroid gland, especially the acute manifestations, are ascribed to the simultaneous removal of the epithelial bodies known as parathyroids. They are four in number. I do not know of a statement dealing directly with the question how much of the parathyroids has to be removed in order to bring out the pathologic effects. However, in the dog the parathyroids are imbedded in the thyroids, two in each lobe, and some of the acute symptoms following the removal of the thyroids in dogs are ascribed as stated above, to the simultaneous removal of the parathyroids. By the removal of four-fifths of the thyroids, surely two and probably three of the parathyroids are also removed. But since the removal of four-fifths of the dog's thyroids is not attended with any evil consequences, we may also conclude that a good deal of the substance of the parathyroids can be dispensed with without any ill effects.

For the suprarenal glands it is now well established that their removal is absolutely fatal to the animal. Death follows within eight to thirty-six hours after the extirpation of the glands under conditions of low blood pressure, extreme muscular weakness and exhaustion. But the removal has to be complete; if one-tenth of the glands or even less is left in the body, the animal shows no pathologic symptoms. Here, again, as in the thyroid, this fact caused the divergence of opinion which sprang up soon after Brown-Séquard made the discovery of the importance of this ductless organ. In many of the experiments bits of the tissue of that organ were left behind; besides, many an animal hides, somewhere, accessory organs of the same type. For the adrenals, then, it is evident that the body possesses indispensable tissue at least ten times as much as is necessary for the maintenance of normal life.

The brain is built on a bilateral plan. In former years, when, following the lead of Flourens and as a reaction to the teachings of Goll, the brain was considered as a uniform organ, attending only to one function, some facts seemed to demonstrate indeed that there is a great excess of tissue in that organ, since the older experiments of Flourens and newer experiments of Goltz indicated that large parts of the brain could be removed without serious injury to life. To-day we know that the brain presents a collection of many organs, of many centers, the injury of each of which is followed by sensory or motor disturbances in definite areas of the body. As a whole, the bilateralness of the hemispheres does not mean the same as bilateralness in other organs, namely, a duplication of tissue for one and the same function. One hemisphere attends to the needs of one side; for instance, the motor areas of the right arm or right leg are located in the cortex of the left hemisphere, and those of the left arm and left leg are located in the right hemisphere. The same is true of the subcortical centers and apparently also of the medulla oblongata.

To this rule there is, however, an exception for the motor organs having in charge such muscles or group of muscles which normally contract on both sides simultaneously. The motor area of one side can take charge of the muscles of both sides. Such is the case with the motor areas of the respiratory muscles, the muscles of the larynx, of deglutition, etc. An injury to the motor areas of these muscles in one hemisphere only does not cause paralysis of these muscles. An instance well known to practitioners is the one-sided injury to the motor area of the orbicularis palpebrarum. The muscle, as a rule, is not paralyzed by such an injury, at least not when the muscles on both sides contract simultaneously. As is well known, the absence or presence of paralysis of this muscle in cases of facial paralysis serves as a means to diagnose whether the paralysis is of central or peripheral origin.

An example of an uneconomical principle, to use the expression of Verworn, we find in the bilateral innervation of certain viscera by the pneumogastric nerves. For instance, the nor-

mal rhythm of respiration is completely changed when both vagi are cut, whereas when only one vagus is cut, the respiration remains normal. Apparently, one vagus nerve is amply sufficient to carry on the regulation of respiration. A similar condition obtains with regard to the heart beats. For certain animals, the dog, for instance, the vagi carry on an inhibitory tonus. When both vagi are cut, the heart beats are considerably increased in frequency; when only one vagus is cut, the rate does not change. Here, again, a single vagus nerve is sufficient to carry on that inhibitory tonus. Still more striking is the following fact: After cutting both vagi, the animal dies within a day or two from aspiration pneumonia, whereas when only one vagus is cut, the animal not only survives the operation, but is for all purposes apparently perfectly normal. One vagus nerve, then, is amply sufficient to carry on all these functions; but the body is provided with two nerves. According to Verworn, this should be an example of a violation of the principle of economy in the animal body and its existence should be denied *a priori*.

EXCESS OF TISSUE IN THE UNSYMMETRICAL ORGAN.

Further examples of the ample provision of the structures of the body with factors of safety we meet also in the organs of the body which are not built on the bilateral plan, the unsymmetrical organs. We shall mention here first the pancreas with respect to its internal secretion. It is now common knowledge that the complete removal of the pancreas leads to glycemia and glycosuria. But here we note the fact that if a small part of the gland, say not more than one-tenth, is left in the body, no ill effects follow such an extirpation. One-tenth of that gland is capable of completely protecting the animal against glycosuria; but the body is nevertheless provided with ten times as much.

Another striking example is the liver. This organ has many important functions. It converts the sugar into glycogen; it converts the poisonous ammonia compounds into the comparatively harmless urea. It forms bile which carries out poisons

from the body, removes waste products, assists in some way or another in the absorption of fats, aids in the digestion of proteids and what not more. But Ponfick found that the removal of one-half of that organ practically does not interfere with the life of the animal, and the successful removal of even three-fourths of the organ does not produce symptoms indicating that any of its functions are seriously interfered with. That organ then is provided with an abundance of active tissue considerably in excess of its normal requirements.

Similar striking examples of factors of safety we meet with in the luxurious construction of the gastro-intestinal canal. The entire stomach or the greatest part of it has been removed in animals and man without interfering with digestion and nutrition. Of the small intestines, large parts have been resected without serious consequences. In human beings the largest part removed measured, I believe, over 3 meters, and Erlanger and Hewlett have studied the metabolism of dogs seven or eight months after the removal of 70 or 80 per cent. of the movable part of the small intestines. Three-fourths, then, of the small intestines are almost a luxury to the body. We need not perhaps speak of the fact that surgeons have removed large parts of the colon without ill effects. From the present attitude of bacteriologists and physiologic chemists toward the activities of the large intestines, one is led to believe that the body might do best without any part of that organ. Be this as it may, it is quite sure that the digestive canal is provided with a good deal more structure than is required for the maintenance of its function.

Here we shall discuss briefly also the luxurious provision of the alimentary canal with digestive ferments. There are two proteolytic ferments, pepsin and trypsin, to which we may add also erepsin, a ferment found by O. Cohnheim in the mucous membrane of the small intestines, and which is said to be capable of splitting albumose into amino acids. There are two amylolytic ferments, the ptyalin of the salivary glands and the amylopsin of the pancreas. As to lipolytic ferments, the steapsin of the pancreas is not the only one of that kind

which reaches the contents of the digestive canal. Thus several investigators have recently confirmed the statement of Volhard that the fundus of the stomach secretes a lipase which is capable of splitting emulsified fat. Lipase is contained also in the liver and in the bile.

Now, there are a number of experiments and clinical facts which go to show that digestion can continue in normal fashion, even if one-half or at least a good part of these ferments are eliminated from the digestive tract. Older and recent experiments have established the fact that the removal of the salivary glands has no effect on the digestion. We know, on the other hand, that after removal of the pancreas, or in cases of isolated destructive diseases of this organ, the digestion of carbohydrates is not disturbed. Normally, therefore, there is a superabundance of amylase in the digestive canal. As to the proteolytic ferments, we have already mentioned that the complete removal of the stomach does not disturb digestion. Furthermore, in cases of achylia gastrica, in which the stomach secretes neither hydrochloric acid nor pepsin, the proteid digestion is apparently normal. On the other hand, we know that the elimination of the pancreas does not affect palpably the proteid digestion. With regard to lipase, clinical pathology has taught that in cases of disease of the pancreas the stool contained fat, which would seem to indicate that, in the absence of the pancreatic lipase, no other lipolytic ferment was present in sufficient quantity to split completely the ingested fat. However, in a very recent study by Umber and Brugsch it was shown that the fat-splitting function is carried on, even in the absence of the pancreas, in a normal way.

We are, then, surely justified in claiming that the various digestive ferments exist in the alimentary canal in quantities far above the necessities for the digestion of a normal amount of food.

THE EXTRAVAGANCE OF NATURE.

All the numerous organs and complex tissues which we have just passed in review are built on a plan of great luxury.

Some organs possess at least twice as much tissue as even a maximum of normal activity would require. In other organs, especially in those with an internal secretion, the margin of safety amounts sometimes to ten or fifteen times the amount of the actual need. An extreme degree of superabundance and actual wastefulness we meet with in the organs and functions having charge of the continuation of the species. Let us illustrate it by the following few data: The ovum exists for the purpose of reproduction. Assuming that the sexual function of a woman lasts forty years and assuming, further, that every ten months of these years would be taken up by a pregnancy, then only fifty ova would be required of the ovary. But assuming even that a regular menstruation is an essential and indispensable part of the sexual function, then five hundred ova would be the maximum that the function of reproduction could use. Nevertheless, we find that the ovary of the new-born female child possesses between 100,000 and 400,000 eggs, and at the time of puberty there are still about 30,000 ova ready to enter on their possible mission. That is, the ovary contains at puberty sixty times more ova than the body could possibly ever employ. But there is an incomparably greater waste in the provision of the male germ. According to Rohde, each ejaculation contains 226,000,000 of spermatozoa. Now, we know that of all these legions only one single spermatozoön is required and only one can be used. What a marvelous waste of living cells for the sake of assuring the perpetuation of the species. But there are some attenuating circumstances. With a velocity of only 0.06 of a millimeter per second, with the dangers of crossing the sea of fatal acid vaginal secretions and with a resistance to the onward swaying in the opposite direction, not too many of the storming millions stay in the race and have a chance to reach the goal. At any rate, it is not by economy, but by immense waste of cell life that the chance for continuation of the species is assured.

In striking contrast to the extreme luxuriousness of provision of tissue in the organs previously described stands out the

comparative scantiness of cell tissue in some organs—if we may call them so—of the central nervous tissue. The centers of the medulla oblongata, for instance, present such minute bodies that hardly a part of any center could be injured without endangering the entire function. Any injury to the respiratory center suspends immediately and permanently the function of respiration. The possible existence of some respiratory centers in the spinal cord does not alter the practical result. The same applies to the center of deglutition. The blood pressure, as we shall see later, is provided with quite a large number of safety factors. However, the immediate effect of an injury to the vasomotor center is a dangerous drop in blood pressure, the restitutions and compensations over which the mechanism commands are not forthcoming until after a long interval. We may point out, however, that the central nervous system is provided externally with factors of safety against two of its main enemies: it is protected by a bony encasement against any physical injury, and especially is the medulla oblongata well hidden away, and it is protected by an abundance of blood vessels against dangers of anemia.

Following the old divisions of the organs of animal life into reproductive, vegetative and animal systems, we may say, perhaps, that the reproductive system is provided most and the animal system is provided least with factors of safety, while in the vegetative system, which in that regard occupies a middle position, those organs which seem to be less well differentiated, like the organs for internal secretion, seem to be provided with a larger surplus of tissue.

FACTORS OF SAFETY IN THE CIRCULATORY APPARATUS.

The complex apparatus of circulation is well provided with factors of safety. In the first place, the animal body possesses a good deal more blood than it requires for its work. It is known by experimental evidence and clinical observations that nearly one-half of the blood can be withdrawn without serious consequences to the life of the animal. As a further factor

of safety in this regard we might register the ability of the blood to recover its loss very rapidly.

Furthermore, the capacity of the entire system of blood vessels in a completely relaxed state is again much greater than the volume of blood of the body. It is this difference between the volume of blood and the volume of the vessels which greatly facilitates the circulation of the blood and the proper nutrition of the various organs of the body. On the basis of this difference large quantities of blood can be thrown at once and with ease into the splanchnic region, into the skin or into the working muscles. After a local injury or infection in a very brief time for the sake of repair or defense hyperemia sets in, and vessels which were not noticeable before become fairly visible. An instance of a similar order is the widespread institution of collateral circulation. Around an anemic focus blood vessels which previously were hardly visible become full and large to meet the threatening danger of necrosis of the neighboring anemic tissues. All these devices which spring into activity only under special exigencies are manifestly factors of safety and are made possible by superabundance of blood vessels.

The difference between blood volume and capacity of vessels is an indispensable factor of the circulation, and its permanence is assured by many devices. Thus, for instance, any artificial increase of the volume of blood is immediately corrected through the chief eliminating organs, or through the secretory glands, or even by throwing some of the surplus serous fluid temporarily into the lymph spaces and serous cavities. Edema, ascites and hydrothorax are sometimes not parts of the affliction, but means of repair.

Furthermore, existence of the difference between vascular capacity and quantity of blood is made possible only by a wonderful mechanism which controls in every part of the body the mutual adaptation of blood and vessel—the so-called vasomotor apparatus. It causes the dilatation of the vessels in the part of the body which requires and is to receive more blood, at the same time causing a constriction of the vessels

in a part which can spare some of its blood. This mechanism is so important that it is again guarded by an abundance of factors to assure its safety. There is a vasomotor center in the medulla oblongata; when this is destroyed a number of vasomotor centers in the dorsal medulla assume control; when they are eliminated the sympathetic ganglia take over the command, and when they too drop out the vascular wall itself attends to the proper regulation and adaptation of the capacity of the vessels to the volume of blood.

Finally, the chief motor mechanism of the circulation, the heart, is a clear instance of an organ provided with a superabundance of volume and force. Normally it is in a state of tonus and receives only a moderate volume of blood which it throws into the aorta with no great hurry and with an expenditure of only a moderate amount of energy. But at any moment it is ready to receive many times the usual volume of blood, is ready to double or treble the rate of its beats and is capable of developing nearly any amount of energy which the situation might require of it. It is a wonderful, prompt, adaptive motor mechanism with a good reserve of force.

We have, then, in the circulatory system many instances of provisions with factors of safety to assure the nutrition of all parts of the body in all states and conditions. An abundance of blood, a superabundance of blood vessels, a vast provision of factors for the safety of the adaptation of the two to one another and a great reserve of motor force for transportation and distribution of the blood.

The multiple mechanisms existing for the care of the vasomotor apparatus lead us to the following considerations: The internal motor organs of the body, like the gastro-intestinal canal, the heart, the uterus, etc., are provided with central motor innervations as well as with local motor mechanisms. In all cases it has been shown that the movements of the organs continue also after the severance of the connections with the central nervous system. Thus the heart continues beating after section of both vagus and accelerator nerves, the peristalsis of stomach and intestines continues after cutting the

vagi and the splanchnics, and pregnancy and delivery take a normal course after complete destruction of the spinal cord.

On the basis of these facts it is now generally assumed that the extrinsic innervations of these organs have only a regulating function, while the real motor function is invested in peripheral devices, be they of neurogenic or myogenic character. This conclusion is obviously based on the supposition that the function of an organ is carried on only by a single mechanism. Hence the fact that the motor work is carried on after eliminating the extrinsic nerves seems to be sufficient evidence that they can not form an integral part of the motor function.

These conclusions are fallacious. There are an abundance of instances in which one and the same function is cared for by more than one mechanism. But we need only refer to the vasomotor apparatus. It was known before, and it has been very recently conclusively demonstrated again by Magnus, that after eliminating the influences of the sympathetic and the central nervous system the blood pressure is well taken care of by the peripheral mechanism of the walls of the blood vessels. Nevertheless, nobody doubts that the vasomotor centers are integral parts of the vasomotor mechanism. Why this difference of views for the different organs of the body?

The subject is evidently an important one; but we shall not enter into a further discussion of it. The remarks were made to illustrate the importance of the conception that in the animal body one function is not infrequently cared for by more than one mechanism. It is capable of profoundly affecting the views on many vital biologic problems.

DUPLICATION OF MECHANISMS AND ORGANS.

We shall cite a few more instances in which two or more parallel mechanisms exist for the accomplishment of one function. I may be permitted to mention in the first place the function of deglutition. As was shown by us about twenty-five years ago, fluids and semifluids are squirted down from the mouth to the cardia by the force of the contraction of the

mylo-hyoid muscles, but they can also be carried down by the peristalsis of the esophagus. Of the latter there are again, as I have recently shown, two kinds: a primary peristalsis which runs independently of the integrity of the esophagus and a secondary peristalsis which is closely connected with the integrity of the tube and which is more resistant to certain detrimental influences. It will probably be shown before long that the esophageal wall alone is also capable of contributing to the function of carrying the food down to the stomach.

The functions of the pancreatic secretion seem to be an instance in which mechanisms of a different type are sharing in its management. It has long been established that the pancreatic secretion stands under the influence of the central nervous system. Recently it was discovered by Bayliss and Starling that an intravenous injection of secretin causes a considerable increase of pancreatic secretion. Secretin is an extract made of the duodenal mucosa with an addition of hydrochloric acid. It is assumed that this substance is produced normally when the acid chyme comes in contact with the mucosa of the duodenum, and that by its absorption into the circulation it is one of the normal causes of pancreatic secretion. Now, the effect of the secretin seems to have nothing to do with the nervous system, since the injection is active even after all connections with the nervous system are destroyed. On the other hand, in cases of achylia gastrica, in which the stomach is devoid of all secretion, the pancreatic secretion is apparently normal, as the digestion of proteids remains undisturbed. But since in these cases there is no secretion of hydrochloric acid, secretin ought to be absent; here the pancreatic secretion is probably attended to properly by the other partner in the management of the function; that is, by the central nervous system.

A double management of partners of a different type exists probably also for the mammary secretion. There is sufficient evidence that the secretion of milk is under the influence of the nervous system. Nevertheless, the secretion continues after all nerves going to the mammary gland are cut. The milk

secretion in the latter case is probably kept up by a stimulation through an internal secretion provided by the reproductive organs. Internal secretion is probably a co-existing factor in many functions of the body.

Furthermore, there are instances in which one function is cared for by two separate organs. The function of digestion of proteids in the alimentary canal is carried on by two separate organs with a different chemical activity: the pancreas and the stomach. The trypsin of the pancreas digests proteids in an alkaline medium, while the pepsin of the stomach is active only in an acid medium.

An arrangement of a similar character we meet with in the organization of the function of the defense of the body carried on by the white cells against foreign invaders. This cellular army of defense is made up of two types: the microphages, the polynuclear leucocytes whose abode is in the bone marrow, and the macrophages, the large mononuclear cells which have their barracks in the lymph nodes and lymphoid tissue. According to Opie, one of the effectual weapons of these warriors is their intracellular proteolytic ferments. But the ferment of the microphage is active in an alkaline medium, while that of the macrophage requires for its activity an acid medium.

As factors of safety we may consider also the assistance which one organ lends to another or the vicariation of one organ for another. For instance, the assistance which the sweat glands render to the kidney in the process of elimination of a surplus of water, or the vicariation of the mucous membrane of the intestinal canal in the process of elimination of urea. Such mutual assistance of the organs is a widespread institution in the animal body and assures the safety of many vital functions.

MODE OF DISTRIBUTION OF THE ACTIVITY AMONG THE TISSUES.

Returning to the organs which are provided with a large surplus of active tissue, the question confronts us: Which is the mode of distribution of the normal activity of an organ among its luxurious tissues? Since the activity of such organs,

as we have seen, is far below the capacity of their tissues, the distribution could occur only in two ways. Either some part of the tissues work to their full capacity, while the other parts remain idle, being only in readiness for emergencies—like the unemployed vice-president of some organization—or all elements of the organ take equal part in the work, each tissue-element employing only a fraction of its capacity for work. The last alternative is probably the more frequent mode of distribution. There are, for instance, probably no totally inactive glomeruli and tubules in the kidneys, no inactive liver cells, no thyroid epithelial cells entirely without colloidal substance, but the epithelium of the glomeruli and tubules work only one-half of their capacity, the islands of Langerhans work less than one-tenth, the vesicles of the thyroid about one-sixth of their capacity, etc. For the muscles of the heart it is generally assumed that all the fibers take part in every contraction, but that they work normally only a fraction of their capacity. On the other hand, there are organs in which surely parts of the tissue do not take active share in the work, unless called on under special circumstances. In the ovaries, for instance, surely only one ovum becomes fertilized, while all the others are only on the waiting list. An instructive instance is the mode of distribution of work among the respiratory muscles. In normal inspirations, for instance, we find only the diaphragm alone at work. When somewhat deeper breathing is required, the inspirations are supported by the levatores costarum and the scaleni. Furthermore, in labored respirations also the sternohyoid and the posterior superior serrati become engaged in the work, and when the difficulties become still greater still other groups of muscles enter into the struggle. In other words, the different groups of muscles which are designated to do the work of inspiration are not engaged in it in the manner of partners of equal standing, but enter on their duties as a series of vice-presidents, or, rather, as a series of reserve forces. On the other hand, in the diaphragm probably all the muscle fibers are engaged in the work of each inspiration at all times, employing only a fraction of their capacity in

normal or shallow inspiration and working to their utmost capacity in dyspnea or asphyxia. We see, therefore, in one and the same function both modes of distribution of work well represented, one muscle steadily at work with all fibers, like a heart, adapting the degrees of their energies to the various requirements of their work, and a number of groups of other muscles, acting as graded reserve forces, idle but ready for emergencies—instructive examples of luxurious factors of safety.

In the foregoing we have brought forward a sufficient number of instances in which various parts of the living organism are provided with a superabundance of material and energy to warrant the comparison of the organism with a machine with regard to the provision with factors of safety.

FACTORS OF SAFETY FOR THE FACTORS OF SAFETY.

One of the fundamental differences between living organisms and human-made machines is that the former carries in it the germ for self-propagation, while machines have to be made by human hands. As a further difference between the two constructions we may perhaps consider the phenomenon of self-repair. Possibly the phenomenon of self-repair in the organism is closely allied with the phenomenon of self-propagation. The same source which provides the organism with a mechanism for a reproduction of the entire body provides its parts with a mechanism for regeneration of these parts. Reproduction and regeneration might have a common cause. At any rate, self-repair distinguishes the organism from the machine. If parts of a machine yield to stress and the factors of safety become exhausted, the machine would surely break down, unless it is repaired by human hands, just as it is made by human hands. As far as I know, no machine has yet been invented which is provided with devices for a continual self-repair. In the living organism self-repair is a widespread function of living tissues and organs. It is a dormant force, a reserve force, which springs into immediate activity as soon as any injury is inflicted. It is a factor of safety peculiar

to the living organism. It manifests itself in the forms of regeneration and hypertrophy of tissues and organs, and also in the functional forms of inflammatory reaction, of substitution, vicariation and adaptation. And here it is interesting to observe that self-repair does not set in only when the margin of safety is exhausted, when there is an actual need for repair, but begins when only the integrity of the factors of safety is encroached on. Self-repair is a factor of safety also for the protection of the factors of safety. When, for instance, one kidney is removed, the hypertrophy of the secreting elements begins a few hours later, although the urinary secretion was hardly impaired. It is an attempt to reprovide with luxurious tissue. The liver cells regenerate, the thyroid, the adrenals and other organs hypertrophy and regenerate even when the preceding injury was not extensive enough to affect the function of these organs. It is, as stated before, an attempt to restore the factors of safety. A heart working above normal becomes hypertrophied even if it has not yet met with any obstacles; it is a provision in time against possible shortcomings; it is a repair of the factors of safety. This is a very interesting field, but it would lead us too far to enter on a detailed discussion of the various aspects of the subject.

TWO EXCEPTIONS.

We would only call attention to two exceptions. One is the very scanty repair which takes place in the organs of reproduction. But the affluence is here so immense that the organs may safely forego the benefits of self-repair. The other exception concerns the nerve ganglia; nerve cells, as a whole, do not regenerate. We have learned above that the ganglionic masses of the central nervous system are scantily provided with factors of safety. Here we learn that they are also deprived of the great aid afforded by regeneration. There is some functional self-repair in the central nervous system. Other centers assume the work of the lost ones; adjacent tissues become educated to the work; dormant centers of the opposite hemispheres awake gradually to their new missions. But all these

substitutes are insufficient to replace satisfactorily the lost function, not to speak of a provision for factors of safety.

Here we must recall that the lack of regeneration applies only to the nerve cells. The nerve fibers, on the other hand, especially those of the peripheral nerves, show rather a very active regeneration.

The foregoing review shows, I believe, conclusively, that the tissues and organs of the living animal organism are abundantly provided with factors of safety. The active tissues of most of the organs exceed greatly what is needed for the normal function of these organs. In some organs the surplus amounts to five, ten or even fifteen times the quantity representing the actual requirement. In the organs of reproduction the superabundance and waste of tissue for the sake of assuring the success of the function is marvelous. Furthermore, the potential energies with which some organs, like the heart, diaphragm, etc., are endowed are very abundant and exceed by far the needs for the activities of normal life. The mechanisms of many functions are doubled and trebled to insure the prompt working of the function. In many cases the assistance of one organ is assured by the ready assistance offered by other organs. The continuance of the factors of safety is again protected by the mechanisms of self-repair peculiar to the living organism. We may, then, safely state that the structural provisions of the living organism are not built on the principle of economy. On the contrary, the superabundance of tissues and mechanisms indicates clearly that safety is the goal of the animal organism. We may safely state that the living animal organism is provided in its structures with factors of safety at least as abundantly as any human-made machine.

ECONOMY OF EXPENDITURE AS A FACTOR OF SAFETY.

The safety of a mechanism is increased, as we have stated before, also by an economic handling of the expenditure of its energy. The expenditure of energy by the living animal organism consists chiefly in the work which it performs, that is,

the contraction of the muscles. Of the involuntary work of the body it is only the action of the heart and the respiratory muscles of which we possess a knowledge of some available facts. The heart, although capable of doing a great amount of work, is normally kept down to perform only the most indispensable duty. The inhibitory tonus exercised by the vagi prevents the heart from beating too rapidly and too strongly when it is not required, and the vascular reflexes carried from the heart or aorta to the vasomotor centers regulate the vascular circulation so as not to offer too much resistance on the one hand and not to fill up the heart with too much blood on the other hand.

The respiration is normally carried out only by one muscle, the diaphragm, and this works only with a fraction of its capacity, the distension of the lungs producing an inhibitory stimulus preventing the muscle from overaction.

The contractions of the skeletal muscles being regulated chiefly by the will offer insufficient opportunities for a study of the normal regulation of expenditure of energy emanating from this source. There are, however, two facts which are instructive and deserve to be mentioned. One is the provision of the muscle with the sense of fatigue setting in with overexertion; it might serve as a guard against overwork, against exhaustion of the muscles. The second fact is the provision of the muscular innervation with inhibitory impulses for antagonistic muscles; it prevents harmful or even only unnecessary contractions. In other words, it prevents the muscles from an unnecessary expenditure of energy. While the facts are not many, they are sufficient to indicate the tendency of the organism to be economical in its expenditure of energy.

FACTORS OF SAFETY IN THE SUPPLY OF ENERGY.

We now arrive at the examination of the principles governing the supply of the organism with energy. A machine is provided with fuel far above the necessity for the performance of the expected minimum work; it has to be in readiness for unforseen exigencies. How about the organism? The

supplies for the animal machine consist of inorganic salts, water, oxygen and food. Our knowledge of the laws governing the supply and expenditure of water and inorganic salts for the animal organism are still too imperfect to be utilized here for the elucidation of our problem. We have to restrict our discussion to the supply of food and oxygen. The supply of food is influenced so much by the will of the animal that it is difficult to obtain facts permitting only one interpretation. For instance, the amounts of food taken by men in all parts of the world cannot be taken as the normal quantity which the body requires, because, as Chittenden and his school say, this amount is dictated by habit and not by actual necessity. The latter found, as stated before, that with a proteid diet lower than the one employed in the current diet of man, a number of men continued their normal life without special incidents. As a result of this observation these investigators assume that the minimum proteid diet is the normal one and advocate its adoption as a standard diet.

The finding that men can continue to live with a certain minimum is a fact; the assumption that this minimum is the actual requirement of the organism is, however, only a theory, and a theory which decides that, in contrast to a human-made machine, the animal machine should be provided with a minimum supply of energy just sufficient for the average daily incidents and daily work. Neither can we, on the other hand, look on the facts which we have brought together as an absolute proof that the animal's supply of energy ought also to be provided on the same plan of superabundance. It may be claimed that the animal's welfare is best cared for by observing stringent economy in the supply of its energy.

SURPLUS OF OXYGEN.

Luckily, however, the supply of oxygen to the organism is a process practically entirely independent of the will, and, therefore, a fact or two which we find here may well throw some light on our problem. One fact here is, indeed, instructive. It is a frequently made and well-established observation

that the oxygen of the inspired air may be reduced to about one-half of its normal amount without causing any ill effects whatsoever. The oxygen of the atmospheric air amounts to about 21 per cent., and it may safely be reduced to about 11 per cent. or 10 per cent. Nature, then, supplies oxygen to the animal body in an abundance, amounting at least to twice the maximum quantity which the normal condition of life may require.

Furthermore, even with an atmosphere greatly reduced in oxygen, the body is capable of attending to work so strenuous that it may cause a consumption of oxygen perhaps five times the amount normally used up during rest or light work. This occurs, as was demonstrated in the interesting experiments of Zuntz and his co-laborers in climbing mountains and carrying at the same time considerable loads at altitudes with a barometric pressure of less than 500 millimeters of mercury. We should also remember another instructive and characteristic fact, namely, that the venous blood is comparatively still rich in oxygen, possessing often nearly two-thirds of that present in the arterial blood, which means that the oxygen carried in the arterial and capillary blood is greatly in excess of the requirements of the cellular tissues.

Finally, another interesting point is that labored breathing sets in long before the tissues are in actual need of oxygen. Dyspneic breathing is a device to cause a refilling of the exhausted surplus of oxygen by a more efficient pulmonary ventilation. The hard working skeletal muscles which consume an undue amount of oxygen produce at the same time a substance which stimulates the respiratory center to greater activity and thus to a more liberal provision of oxygen. This is, again, a sort of self-repair of the loss to the factors of safety. All this is sufficient evidence that, as far as the oxygen is concerned, the supply of the body with energy is certainly not conducted on the principle of stringent economy. On the contrary, abundance is the guiding rule here, as it is in the provisions of the body's structures.

We now again return to the question of supply of food.

The presence of an abundant supply of glycogen and fat in all animal bodies seems to me to be a sufficient indication that carbohydrates and fats are not supplied on the principle of stringent economy. Fuel material is here abundantly stored up, not so much for its immediate use, but essentially for use in unforeseen exigencies. As far as I know the claim has not yet been raised that these savings deposits are due only to acquired habits of ingesting too much of the mentioned forms of food.

With regard to the proteid diet, however, the question of the normal supply, as we have repeatedly mentioned, is not above discussion. In a recent review of the subject by Benedict one of his precise statements reads: "Dietary studies all over the world show that in communities where productive power, enterprise and civilization are at their highest, man has instinctively and independently selected liberal rather than small quantities of protein." Chittenden, on the other hand, says: "All our (experimental) observations agree in showing that it is quite possible to reduce with safety the extent of proteid catabolism to one-third or one-half that generally considered essential to life and health." And then adds: "It is obvious . . . that the smallest amount of food that will serve to maintain bodily and mental vigor . . . is the ideal." As valuable as the facts which Chittenden and his co-laborers found may be, they do not make obvious their theory that the minimum supply is the optimum—the ideal. The bodily health and vigor which people with one kidney still enjoy does not make the possession of only one kidney an ideal condition. The finding that the accepted standard of proteid diet can be reduced to one-half can be compared with the finding that the inspired oxygen can be reduced to one-half without affecting the health and comfort of the individual. But nobody deduces from the latter fact that the breathing of air so rarified would be the ideal. Chittenden suggests that a greater use of proteid might be the cause of many ills, for instance, of gout and even of tuberculosis and cancer. I shall not attempt to discuss the merits of this theory as far as the

causation of tuberculosis and cancer is concerned. As to the causation of gout, one of Chittenden's most able supporters, Otto Folin, has pointed out that, at best, this could be claimed only for eating crude meat, but not for an ingestion of protein in general, because the latter becomes converted into harmless urea, as Folin says. I would add that if we should avoid eating meat because some of us might sometimes get gout we should surely avoid eating carbohydrates because it sometimes leads to diabetes, and avoid eating fats because it often leads to various mischiefs. What, then, shall we eat with absolute impunity?

But I wish to recall one fact, namely, that the administration of too large a dose of thyroid extract leads to a pathologic condition similar in character to that of Graves' disease. The normal body, nevertheless, possesses, as we have shown above, a great surplus of thyroid tissue without causing any thyroidism. That some isolated metabolic product might do some harm when artificially incorporated into an animal is far from being fair evidence that this normal product of the animal mechanism does harm there when in its normal connections. Metabolic products are present in great abundance in all healthy individuals without causing mischief.

STORAGE OF PROTEID.

The situation seems to me to be this: All organs of the body are built on the plan of superabundance of structures and energy. Of the supplies of energy to the animal we see that oxygen is luxuriously supplied. The supply of carbohydrates and fats is apparently large enough to keep up a steady luxurious surplus. For the supply of proteid we find in the actual conditions of life that man and beast, if they can afford, provide themselves with quantities which physiologic chemists call liberal. This may or may not be the quantity of which Nature requires and approves. Experiments have shown that a number of men subsisted on half of such quantities. This latter might be an indispensable minimum, just as there is an indispensable minimum for all other luxuriously endowed provi-

sions of the animal organism, and the liberal ingestion of proteid might be another instance of the principle of abundance ruling the structures and energies of the animal body. There is, however, a theory that in just this single instance the minimum is meant by Nature to be also the optimum. But it is a theory for the support of which there is not a single fact. On the contrary, some facts seem to indicate that Nature meant differently. Such facts are, for instance, the abundance of proteolytic enzymes in the digestive canal and the great capacity of the canal for absorption of proteids. Such luxurious provision for digestion and absorption of proteids is fair evidence that Nature expects the organism to make liberal use of them. Then there is a fact that proteid material is stored away for use in emergencies, just as carbohydrates and fats are stored away. In starvation nitrogenous products continue to be eliminated in the urine which, according to Folin, are derived from exogenous sources, that is, from ingested proteid and not from broken-down organ tissues. An interesting example of storing away of proteid for future use is seen in the muscles of the salmon before they leave the sea for the river to spawn. According to Miescher the muscles are then large and the reproductive organs are small. In the river, where the animals have to starve, the reproductive organs become large, while the muscles waste away. Here, in time of affluence, the muscles store up nutritive material for the purpose of maintaining the life of the animal during starvation and of assisting in the function of reproduction. This instance seems to me to be quite a good illustration of the rôle which the factor of safety plays also in the function of the supply of the body with proteid food. The storing away of proteid, like the storing away of glycogen and fat, for use in expected and unexpected exceptional conditions is exactly like the superabundance of tissue in an organ of an animal or like an extra beam in the support of a building or a bridge—a factor of safety.

I, therefore, believe that with regard to the function of supply of tissue and energy by means of proteid food Nature meant it should be governed by the same principle of affluence

which governs the entire construction of the animal for the safety of its life and the perpetuation of its species.

Before concluding I wish to add the following remark: It seems to me that the factors of safety have an important place in the process of natural selection. Those species which are provided with an abundance of useful structure and energy and are prepared to meet many emergencies are best fitted to survive in the struggle for existence.