frog, in order to obtain strictly pure inhibitory action. In the frog the accelerator fibres do not join the vagus until the latter has left the cranium. If the vagus is

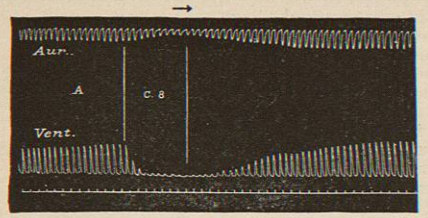

FIG. 2811.—Heart of Frog. Stimulation of vago-sympathetic nerve. Weak current. (Gaskell.)

stimulated just within the cranium, or intracranially, the inhibitory fibres only are excited; while extracranial stimulation of the vagus (or vago-sympathetic), on account of the accelerator fibres which have joined it, give somewhat variable results according to the proportion of the two kinds of fibres in it.

Employing intracranial stimulation of the vagus, Gaskell has noted three interesting differences as contrasted with extracranial stimulation. In the first place, he has been able to obtain absolute standstill of the heart with a strength of current immensely weaker than is required to produce any effect when the vago-sympathetic is stimulated. In the second place, he noticed that the cardiac standstill lasted for a surprisingly long period after discontinuance of stimulation. In one of his experiments in which the vagus was excited intracranially for thirty-eight seconds, the heart remained absolutely still for two hundred and ninety seconds, or for two hundred and fifty-two seconds *after* the stimulus was removed. In the third place, it was possible to keep the heart absolutely quiet for a much longer time than when the vagus was stimulated in the ordinary manner. The frog heart has been kept entirely quiescent for as long a period as twenty-eight minutes with a continued weak intracranial excitation of the vagus. The heart, under these conditions (absence of accelerator fibres), apparently loses or has greatly retarded its power to "escape" from the inhibitory effects.

According to McWilliam, there are three conceivable causes for stoppage of the ventricle to be considered in connection with the arrest of its rhythmic action as a result of vagus excitation: 1. The absence of those incitations to contraction which normally determine the ventricular sequence—such absence being due (*a*) to a cessation of the auricular beats which normally lead off the ventricular beats, or (*b*) to a block in the propagation of the contraction from auricles to ventricles. 2. An inhibitory influence acting through the vagus nerve on the inherent rhythmic property of the ventricles. 3. A combination of the two preceding conditions.

Cardio-Inhibitory Centre.—It is assumed by many observers that this centre in the oblongata is in a state of

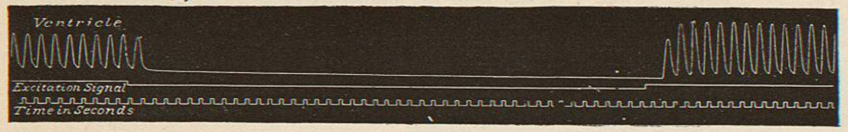

FIG. 2812.—Heart of Toad. Long stimulation of the intracranial roots of the vagus with moderately strong current. (Gaskell.)

tonic excitement; that there is a continuous, uninterrupted, regulating, and inhibitory action of this centre upon the heart through the fibres of the vagus.

Direct Excitation of the Centre.—Sudden anæmia of the oblongata, by ligation of both carotids and subclavians, causes slowing and even temporary arrest of the action of the heart; sudden venous hyperæmia acts in a similar manner, and can be produced by ligating all the veins coming from the head; an increased amount of CO_2 in the blood, produced either by direct cessation of the respiration or by forcing into the lungs a quantity of air containing much CO_2, will also stimulate this centre; excitation is also produced by an increased blood pressure in the cerebral arteries.

Reflex Excitation of the Centre.—This may occur by stimulation of sensory nerves or nerves containing afferent fibres, *e.g.*, the sciatic (stimulation of the central end of this nerve will slow the heart's action); by stimulation of the central end of one vagus, provided the other vagus is intact; and by stimulation of the sensory nerves of the intestines through tapping upon the belly, or by direct excitation of the splanchnic or of the abdominal or cervical sympathetic. Goltz's experiment succeeds very readily by tapping the intestines of a frog with the handle of a scalpel, especially if the intestine has been exposed to the air for a short time, so as to become inflamed. The reflex arc for this effect is formed by the abdominal sympathetic, the spinal cord and bulb, and the vagi. Almost any form of stimulation of the abdominal viscera

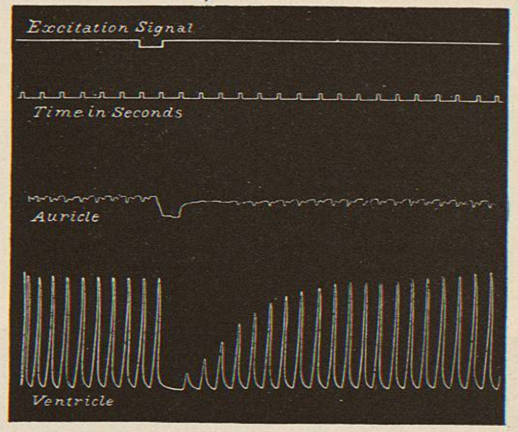

FIG. 2813.—Heart of Toad. Short stimulation of the intracranial vagus roots with current of moderate strength. The change in level of the auricular tracing is due to the movement of the laryngeal and trapezius muscles. (Gaskell.)

produces slowing of the heart. Sudden distention of the stomach may be referred to especially as provoking a reflex of this character. Starvation renders the vagus centre much more excitable.

According to François-Franck, stimulation of the mucous membrane of the lungs and the upper part of the larynx causes slowing of the heart. Excitation of the nasal branch of the fifth nerve always diminishes the frequency of the pulse. Cardiac inhibition is therefore of usual occurrence during the primary stage of inhalation of chloroform or ammonia.

A condition of high intracardiac pressure has been found to render vagus inhibition more difficult, and again, beyond certain limits the arterial pressure cannot be greatly raised, so long as the vagi are intact. There is apparently much to be said in favor of the idea that the terminations of the afferent

nerves on the inner wall of the heart may be stimulated by intracardiac pressure, and thus the controlling centres of the circulation as a whole—vagus, vaso-motor, and respiratory—excited or depressed. If this be true, the heart possesses a mechanism for regulating reflexly, not only its own rate, but the whole circulatory system.

The cardio-inhibitory centre can be excited not only by the character of the blood which comes into contact with

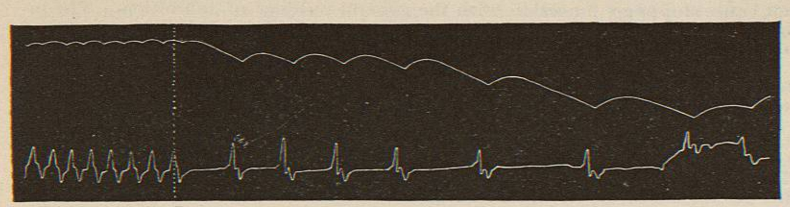

FIG. 2814.—Reflex Inhibition Produced by Inhalation of Ammonia. The upper line is a tracing of arterial pressure, the lower line that of the pulse. (François-Franck.)

it, and by stimulation of afferent nerves (reflex), but also by cerebral stimuli. As is well known, the pulse can be altered by psychical and emotional conditions, and in hypnotic subjects the pulse rate has been observed to undergo a marked change under the influence of suggestion.

Search has been made on the surface of the cerebrum by cortical excitation, to discover if areas were present which might influence the cardiac centre. If suitable strengths of current were used to avoid the excitation of epileptic fits, François-Franck found that stimulation of the motor area with a weak current accelerated the heart, while a strong current slowed the heart. The heart can also be influenced from other parts of the cerebrum. All the cerebral effects are similar to those excited reflexly by stimulation of afferent nerves. As the vagus centre is supposed to maintain a tonic bridle action over the heart, the question arises as to whether this tonus is kept up reflexly by the reception of afferent impulses or whether the centre possesses automatism, as has been suggested by some.

The vagus has been referred to as the nutritive or trophic nerve of the heart, its supposed action, on account of its inhibitory power, being to retard the katabolic processes going on in the heart and thus favor the anabolic or building-up processes. Granting that the vagus acts directly upon the cardiac muscle, and that the impulses are not annulled in the peripheral fibres, as essentially held by Bernard and others, it would appear that the inhibitory impulses are able to lessen or to stop the chemical change in the tissue which leads to contraction. As this chemical change is accompanied by a setting free of energy, it is spoken of as a disassimilatory or katabolic change, so that inhibitory impulses may be said to lessen or stop some katabolic change in the heart. Beyond this it does not seem safe to go at present.

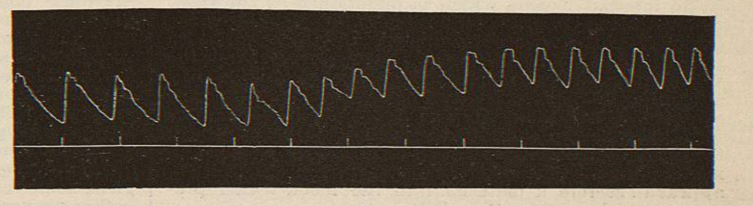

FIG. 2815.—Effect of Sipping Water upon Pulse Frequency; the heart beats faster owing to diminished vagus control, and the blood pressure is raised (man). (Waller.)

It has been implied by some that when anabolism goes on in the cardiac tissue katabolism ceases; that the two processes are mutually antagonistic. This is certainly not the case in the majority of glands in the body, for, as is well known, the two processes go on in these structures actively at the same time. As yet, however, no true inhibitory fibres have been positively shown to exist in the glandular tissues, and it therefore seems to be an open question as to whether anabolism actually stops katabolism in the tissues in which inhibition occurs.

Inhibition Following Regeneration of Vagus.—It is a well-known fact that when both vagi are cut in a mammal, death soon follows the operation. If, however, the two vagi are cut at different times, sufficiently distant from each other, death does not necessarily occur. As in other nerves, when the vagus is cut the fibres peripheral to the cut degenerate. In the regeneration which follows, in the course of time, do the regenerated fibres exhibit the same inhibitory function upon the heart as before? According to the experiments of Tuckett upon rabbits, it seems that an affirmative answer can be given. After the animals were operated upon, three years were allowed to elapse before the vagus was tested. When the nerve thus operated upon was stimulated, it was found that inhibition of the heart occurred, but not so powerfully as under normal conditions, and the conclusion is drawn that the inhibitory fibres will in time, after complete degeneration and subsequent regeneration, recover their function. From other experiments the inference is also drawn that nerve fibres to striated muscles will recover more rapidly and completely than those going to plain or cardiac muscle.

Inhibition as Affected by Physical Condition.—The experiments of Harrington upon the heart of the guinea-pig show that response to vagal excitation differs markedly according to the time of the year when the experiments were carried on. During the fall and early winter the heart, with an average pulsation of 200 per minute, was very resistant to inhibitory stimuli, it being impossible to bring it to a standstill even when a strong current was employed. During late winter and spring, on the other hand, the heart responded very readily to stimuli through the vagus; a current of only moderate strength sufficing to bring it to a standstill. Later it was noticed that the animals did not live very long or that they died during the experiment. Hygienic conditions were not held to be responsible, as animals were obtained from various localities and the results were practically the same in all. The suggestion is made that the different results, according to the season of the year, are due primarily to a difference in physical condition. In the spring there is a probable lack of body tone, a weakened and debilitated system, affecting also the heart, and under these conditions it became more susceptible to inhibitory stimuli than in the fall, when the conditions were reversed.

Action of Drugs upon the Cardio-Inhibitory Mechanism.—Muscarin, by stimulating the cardiac endings of the vagus, causes the heart to stand still in diastole. Atropine applied in solution to the heart (frog) will set aside the muscarin effect and the heart will beat again. In large doses it will paralyze the vagi; large doses of curare will have the same effect. It is said that a very low temperature or high fever will produce a similar action. Digitalin diminishes the number of heart beats by action upon the cardiac muscle and also perhaps the cardio-inhibitory centre in the oblongata. Nicotine first excites the vagus, then rapidly paralyzes it. Hydrocyanic acid has the same effect (Preyer).

Other Forms of Inhibition.—*Vaso-motor Inhibition.*—The suggestions put forth under this heading are tentative, for experimental evidence is lacking to a considerable extent. Nevertheless there are some analogies to cardiac inhibition, and this seems to be the proper place to discuss them. The general conception that stimulation of a nerve connected with a muscle must cause contraction of that muscle encounters an exception in the case of vagal stimulation, which does not cause stoppage of the heart in systole with contraction of the cardiac muscle, but in diastole with relaxation of the muscle—just the opposite condition.

Stimulation of the vaso-constrictor nerves causes contraction of the muscle cells in the walls of the vessel which they supply. The constrictors are also probably concerned in maintaining the tone of the vessel. Stimulation of the vaso-dilators causes dilatation of the wall of the vessels which they innervate. The two kinds of nerve fibres are antagonistic to each other (as are the cardiac accelerator and inhibitory fibres); moreover, both kinds of fibres may occur in the same nerve trunk, and an effect in a given instance will probably depend upon the relative proportion of the kind of fibres present and their susceptibility to stimuli.

One hypothesis that quite naturally suggests itself is that the vaso-dilator fibres inhibit the tonic action of the vaso-constrictors. The difficulty, however, is encountered that the vessels of any organ are dilated to a greater extent by excitation of the vaso-dilators than they are by paralysis of the vaso-constrictors. In spite of the destruction of the vaso-constrictor nerves, the vessels after a period recover their tone. That the tone is not even for a time abolished completely is shown by the fact that a local dilatation can be produced by certain chemical irritants. Thus it seems evident that some peripheral mechanism exists, a mechanism which, it is true, can be paralyzed by the local application of such a drug as chloroform.

Hill suggests that it is highly probable that the vascular muscles are maintained in a state of tone by the tension of the blood within the vessels. This would be, as he suggests, in close analogy with the fact that the heart is excited to contraction by a rise of internal tension. If this hypothesis be accepted, it may then be supposed that the vaso-constrictor nerves increase the excitability of the vascular muscle to the stimulus of blood tension, while the vaso-dilator nerves diminish the excitability. The vaso-dilator fibres would thus be brought into analogy with the cardio-inhibitory nerves. These lessen the irritability of the heart toward the intracardiac tension (Hill and Barnard, *Jour. Physiol.*, 1897) and relax the cardiac muscle.

On this hypothesis, section of the vaso-constrictor nerves abolishes that tonic condition of exalted excitability to internal tension which is maintained by the vaso-motor centre. It does not, however, entirely destroy the excitability of the vascular muscle to tension, and with time the tone is fully restored. On the other hand, the vaso-dilator influence completely relaxes the muscle by altogether inhibiting its excitability to tension. It is conceivable that the quality as well as the tension of the blood may be the exciting cause of vascular tone. An increase in the alkalinity of the blood favors the development of tone. Certain glands, such as the suprarenals, appear to secrete a material into the blood which produces vascular contraction (Hill).

Inhibition of Secretions.—Secretion, in general, is due to two factors: to the blood circulating through the glands, modified to a certain extent by such conditions as blood pressure, rate of flow, etc.; and to the presence of secretory nerve fibres, although the latter have not been satisfactorily demonstrated in all cases. The blood brings to the gland material which, after a certain amount of elaboration, forms a greater or less portion of the secretion.

Assuming that there is some reason in what has been stated regarding vaso-motor inhibition, there seems to be a correlative connection between it and the process of secretion. This, taken in connection with the action of the secretory nerves, means that the changes going on in the gland are influenced by a nervous mechanism which has the power of regulating the chemical activity of the gland, and at times may totally suppress the secretion.

Positive evidence regarding the inhibition of glandular secretions is lacking to a large extent, but the view above set forth provisionally seems to have some connection with the general subject of inhibition. The influences of some drugs and of psychical or emotional phenomena also have a bearing in this direction, especially with regard to the salivary glands.

Inhibition of the Movements of the Stomach.—Openchowski, in 1883, found that the cardiac orifice of the stomach could be dilated by stimulating a nerve at the lower portion of the œsophagus. He called it "nervus dilatator cardiæ." It was found that this nerve was formed by the union of strands from the two vagi. Langley, in 1898, carried the investigation further. His method was to inject curare into a vein, in order to paralyze the motor nerve endings in the striated muscle of the œsophagus. Atropine sulphate was also injected into the vein, in order to weaken the œsophageal motor nerve fibres and to paralyze the inhibitory nerve fibres of the heart. Stimulation of the vagus under these conditions produced inhibition or dilatation of the cardiac sphincter of the stomach. When the above-mentioned drugs were not injected or if atropine alone was used, the experiment failed. The body of the stomach, also the pyloric sphincter, gave variable results. Occasionally there was inhibition (relaxation) of the fundus and of the whole stomach, but this result was by no means constant.

Inhibition of the Movements of the Intestines.—The discordant results obtained as to whether the vagus is a motor or inhibitory nerve to the intestines are probably due to the influence of various disturbing factors, among which may be mentioned the influence of anæsthetics and the exposure and handling of the intestines, with the circulatory changes thereby induced. More important than these, according to Starling, are the inhibitory influences originating either in the higher parts of the intestine and travelling down the intestinal wall, or started by any sensory stimulation of the intestine itself and transmitted reflexly through the cord. Such influences may largely be cut out by cutting both splanchnics and avoiding any lesion above the point observed.

If these precautions be taken, stimulation of the vagus in the neck, after paralysis of the cardio-inhibitory fibres by means of atropine, will always produce an effect upon the intestinal movements; the effect, which may be little marked at first but increases with each succeeding stimulation, is twofold: (1) an inhibition with very short latent period (less than one second), leading to the dropping of one or two beats; and (2) an augmentation of the rhythmic contractions, which gradually develops after the lapse of from ten to thirty seconds, and lasts for some length of time after the cessation of the stimulus. The vagus effect may come on simultaneously at all points of the small intestine, and is not abolished by ligaturing the second part of the duodenum or the upper part of the jejunum. The vagus fibres must therefore reach the intestine at all points, and do not run down from the stomach or duodenum between the two coats (Starling).

Inhibition of Reflex.—As is well known to physiologists, some reflexes may be controlled or at times altogether prevented. The most favorable conditions for a reflex involve the activity of those parts only which form the reflex arc—a sensory surface, afferent nerve, centre, efferent nerve, and the part to which the latter is distributed (muscle or gland). Involvement of any other portion of the central nervous system usually hinders a purely reflex act. Examples of reflex acts are too familiar to make it necessary to mention them. It is a well-known fact that a cough or sneeze may be checked, although the desire to perform the act is wellnigh irresistible. The cerebrum probably excites the greatest inhibitory action over reflexes. The case of Cranmer, the martyr, may be cited as an example. In spite of

the natural tendency, he held his hand in the fire until it was consumed, thus inhibiting the power of reflex.

Inhibition Referred to the Cerebral Cortex.—The power exerted by the cerebrum in inhibiting reflexes, and its action upon the cardio-inhibitory centre, have already been referred to. The cortex is known to possess the power of originating movements; it has also, perhaps, a function no less important, namely, that of inhibiting movement. The restlessness of lunatics, with lack of mental balance, and the restlessness of dogs which have been deprived of their cerebral hemispheres, as shown by the experiments of Goltz, may be due to the diminution or loss of this inhibitory function. The condition of hypnosis may be the result of, or associated with, a temporary total deprivation of volition, due to an increase of the inhibitory function, as suggested by Schäfer.

Bubnoff and Heidenhain (1881) showed that inhibition was an active function of the cortex. They occasionally got arrest of action after weak excitation.

Sherrington (1893) has shown that electrical excitation of certain parts of the cortex may not only, as has long been known, produce contraction of definite muscles, but that simultaneously inhibition of tonically contracted antagonists may also be brought about. It is probable that the inhibitory action, whatever it may be, is exerted upon the lower nerve centres in the cord and bulb (Schäfer).

Inhibition of Pain.—Assuming that pain may actually be inhibited, the sensory side of the nervous system and the cerebrum would represent the parts involved. Kant has described that he learned to inhibit the pains of his gouty attacks. Other instances may be found, but one of the most interesting cases is that of a so-called "painless man," who had been on exhibition in various shows as "the human pin cushion." He was under the observation of, and his case described by, Witmer (1897, "Twentieth Century Practice of Medicine"): "He could be cut with a knife, or stuck with pins and needles, without showing the slightest sign of pain. I have known him to hold a red-hot coin in his hand without wincing, until it had burnt itself deep into the flesh. It is impossible to say positively whether this subject inhibited the expression of pain, or whether he inhibited the pain itself. He said he felt pain on ordinary occasions, when he had not made up his mind to be insensible to pain; but he reported that when once he had decided not to feel the pain of the stimulus, the pain was no longer felt. There were areas of the skin which he could not render insensible to pain. I am inclined to believe he inhibited the sensation of pain and not its external manifestations."

Pierre A. Fish.

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INNERVATION means the nerve supply and nerve control of some part or other of the organism. This definition embraces every kind of nerve influence and includes therefore the exciting as well as the inhibitory action on the part concerned. It moreover includes the activity of all those sensory (afferent) nerves or nerve apparatuses that serve to transmit sensory impulses from the organ concerned to nerve centers of both the peripheral (sympathetic) and the central nervous systems. If, however, any nerve or nerve apparatus, although situated in the immediate vicinity of a given organ or even within the organ itself, has no connection with the elements of the same, and therefore exerts no influence whatever on its function, such nerve or nerve apparatus must be excluded from the "innervation" of this organ. Usually when we speak of the innervation of an organ we include the nerve control of all its tissues. For instance, innervation of the small intestine means the nerve control over its glands, muscles, blood-vessels, and connective tissue, as well as that nerve supply which conveys sensory impressions from the intestine to nerve centres of the peripheral, and central nervous systems. If we speak of the "innervation" of a muscle the term should include the nerve control over its blood-vessels and its sensory supply, although often the motor action on the muscle fibre alone is meant.

Not only the nerves and nerve apparatus directly connected with the part or organ concerned should be included in the definition of its innervation, but also those connected with it more remotely, as long as they have any control over it. For instance, the arm area of the cerebral cortex belongs within the domain of the innervation of the arm, although when speaking of the latter we more frequently have in mind the peripheral nerves and nerve apparatus connected with it.

B. Onuf (Onufrowicz).

I. INSANITY.—(Synonyms: Eng., Mental alienation, lunacy, aberration; Lat., *Insania, insanitas,* from *insanus,* unsound; Fr., *folie, insanité de l'esprit, aliénation mentale;* Ital., *insania, follia, alienazione mentale;* Sp., *insania, locura;* Ger., *Irrsinn, Irresinn, Wahnsinn, Verrücktheit.*)

Definition.—An actual definition of the term "insanity" is seldom found in recent works on psychiatry. The reason for this is, as Tuke* explains: that it is impossible to compass the multitudinous phases of mental disease under one rigid formula. Spitzka has endeavored to cover the ground in a "definition" one hundred and twenty words in length, but admits the futility of any definition except perhaps for medico-legal purposes. Even in the courts, however, a definition of the term is nowadays seldom called for, as most alienists have come to regard it as unwise and prejudicial to their reputation to attempt it. Chapin gives the definition of insanity as "That mental condition characterized by a prolonged change in the usual manner of thinking, acting, and feeling, the result of disease or mental degeneration." This like all other definitions of insanity is not unassailable, but is sufficiently comprehensive for a medico-legal opinion, is easily understood, and is more serviceable than most of the multitude of definitions that were once in vogue.

For further consideration of the subject the reader is referred to the chapters on the *Diagnosis* and the *Medico-Legal Aspects of Insanity* below. *H. R. S.*

II. INSANITY: CLASSIFICATION OF MENTAL DISEASES.—In the sense in which the term is generally used by writers on scientific subjects classification not only implies that the division shall be logical and the characteristics by which it is determined natural, but also at the same time presupposes the existence in the mind of the writer of a specific purpose. (See "Classification." Baldwin's "Dictionary of Psychology.")

Any attempt to classify mental diseases, *i.e.*, to group together those forms which have certain common and distinguishing characteristics, must necessarily be modified by, and to a large extent depend upon, the author's conception of what does and what does not constitute insanity, since it is obvious that the term is used in a purely conventional sense and does not admit of exact definition any more than do the common terms health or disease. Such being the case, it is plain that fundamental distinctions in psychiatry do not exist. The history of medicine as well as that of other sciences shows clearly that the effort to establish artificial distinctions may be fatally antagonistic to the spirit essential for the sound development of scientific investigation and the further advancement of knowledge. As at present we are quite unable

* See Tuke's "Dictionary of Psychological Medicine."