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## THE VEGETATIVE NERVOUS SYSTEM IN RELATION TO GENERAL MEDICINE.\*

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We are just beginning to realize, after many years of study in pathological anatomy, which has heretofore been considered the basis as well as the superstructure of modern medicine, that it fails to explain those conditions which are of most interest to the clinician.<sup>1</sup> Pathological anatomy may acquaint us with the changes in tissue which are produced by the disease process, likewise the changes which result from it; but the gap between these two has been left unbridged. It can be bridged successfully only by an understanding of biochemistry and pathological physiology.

After many years of close study, we are confronted with many facts which we are unable to explain; largely because our field of investigation has been too narrow. The agencies through which the disease process produces its effects throughout the body, have not been sufficiently investigated. In order to understand this phase of medicine, we

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\* Read before the Medical Society of the State of California, San Diego, Cal., April 19, 1917.

1. Pottenger. The Importance of the Study of Pathological Physiology in Internal Medicine; Illustrated by the Analysis of the Symptomatology of Tuberculosis. (Read before the Forty-second Annual Meeting of the Mississippi Valley Medical Association held at Indianapolis, Ind., October, 1916.)

must realize the manner in which the workings of the human body are controlled. The various controls may be classified under sensori-motor; physio-chemical; and psychical. Disturbance in any of these controls alters function and produces functional pathology or a pathological disturbance in the normal physiology.

It is to a better understanding of these various controls of the body that medicine will address itself in the immediate future. They have been omitted heretofore because of their general abstruseness. Our knowledge has been so slight that we felt our inability to understand them; but now that we have advanced in our study of normal physiology; and now that we better understand the pathology underlying disease processes and the effects of the disease processes in body tissues other than those in which the main lesion is located, we are able to trace the relationship between the two in a way that we were unable to do heretofore. The field is not so difficult as would seem at first thought. Many independent observations have been made and many fundamental truths have been already discovered, which, when put together, will greatly elucidate the subject. It will be necessary, however, for medical men to address themselves to this phase of medicine with the same earnestness and the same eagerness for truth, as they have addressed themselves in the past to the problems of physiology, pathological anatomy and general laboratory study.

The pleasure in the study of disease comes from our ability to explain the phenomena observed; and not until we are able to think in terms of visceral neurology, biochemistry and psychical change, shall we be able to explain the facts which present themselves in our every day practice.

At the outset of one's study in this field, it is necessary for him to understand that there will be incomplete answers to many of his questions. Many seemingly contradictory facts will be met. He must not waive aside the whole matter on this account for there are innumerable primary principles which are thoroughly established; and the number of these will increase with increased familiarity with the subject.

Our symposium this afternoon will deal with pathological physiology. We hope to bring before you—not the symptoms and the signs of the disease alone—but we hope to offer a basis for their explanation. A symptom is a disturbance in normal physiological function. As long as function proceeds in its normal way, no symptoms are presented; but when the normal course is altered, then they arise. In medicine we have made the ridiculous mistake in the past of trying to ignore functional disease; we have tried to brush it aside and consider nothing but organic change; but now we have learned that organic change expresses itself in functional derangement, and it is functional derangement that gives the patient most concern and demands study and relief at the hands of the physician. We shall endeavor by the papers here presented to take up two phases of normal physiological control; that of the vegetative nervous system and the endocrine glands. It can be seen then that the foundation for this symposium is normal physiology or an inquiry into the manner in which nature carries on the intricate activities of the body.

In opening the symposium, I shall confine my discussion to the vegetative nervous system. It must be remembered at the outset that there can be no serious change in the equilibrium of the vegetative nervous system without causing disturb-

ances in internal secretions; neither can there be any serious change in internal secretions without disturbing the equilibrium of the vegetative system.

#### THE VEGETATIVE OR INVOLUNTARY NERVOUS SYSTEM.

In order to make my meaning clear. I shall define the terms used in this discussion before proceeding. In speaking of the vegetative nervous system, I mean the same system as is spoken of by various writers as involuntary and autonomic. (The autonomic is also applied by some writers to the *greater vagus* division of the vegetative system.) It is that system which acts without an act of the will. It presides over those body functions which are necessary to life; and which would be endangered were they left to voluntary control.

The vegetative system supplies nerve fibers to the pilo motor muscles and sweat glands; to the gastrointestinal tract and all glands connected with digestion; to the heart and blood vessels; the respiratory mucous membranes and musculature; the genito-urinary system and all of the secretory glands and all smooth muscles of the body.

The vegetative system consists of two divisions which are physiologically antagonistic. The *sympathetic* system, which takes its origin from the thoracic and upper lumbar segments of the cord; and the *greater vagus*, the fibers of which arise from the mid brain, bulb and sacral portion of the cord. The fibers of the *greater vagus* run in the third, seventh, ninth and tenth cranial nerves, and in the pelvic nerve. This division of the vegetative system is sometimes spoken of as the autonomic, but should not be because of the confusion which it fosters, on account of the vegetative system as a whole being called autonomic.

The vagus is the greatest nerve of this system. The vegetative fibers in the third, seventh and ninth cranial nerves, likewise those in the pelvic nerve, have practically the same action as the tenth cranial, usually called the vagus nerve; consequently, I prefer to speak of them collectively<sup>2</sup> (following Eppinger and Hess), as the extended or greater vagus; and by so doing we arrange the fibers of the vegetative system in two divisions in which all of the fibers belonging to each division have similar action, and so that the two divisions as a whole antagonize each other.

In order to make clear the importance of so dividing the vegetative system, it must be understood that wherever the *sympathetic* and the *greater vagus* fibers meet in an organ, their action is antagonistic. It must further be understood that this antagonism preserves equilibrium and is accountable for the normal physiological action of the organ. If the fibers in one system are overstimulated, then a disturbance in physiological action results and symptoms appear.

It must not be thought, however, that every extra stimulus of one division is going to overcome the action of the other division and destroy the normal equilibrium. The normal equilibrium is not so easily upset. An *adequate stimulus* is necessary. An *adequate stimulus* is one which will overcome the action of the opposing nerve. It may be slight in one case and severe in another. The more stable the nerve equilibrium, the greater the stimulus must be before it becomes adequate. Herein lies the explanation of the oft noted fact that one patient shows symptoms easier; or shows more marked symptoms

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2. Eppinger and Hess, *Vagotonia*. (English Trans.) Nervous and Mental Disease Pub. Co., New York, 1915.

than another patient under apparently the same conditions.

#### THE ACTION OF THE SYMPATHETIC AND GREATER VAGUS IN THE IMPORTANT VISCERA.

In order to understand more fully the action of these two systems, it might be well to take up the important organs and show the tendency which will result from overstimulation of each of the divisions of the vegetative system. In the eye, we have the fibers of the *greater vagus* running through the third nerve, stimulation of which produces a contraction of the pupil and ciliary body (accommodation spasm), and a widening of the palpebral fissure. Stimulation of the *sympathetics* on the other hand dilates the pupil and causes contraction of Mueller's muscle, throwing the eyeball forward. Thus we can see that a disturbance in the equilibrium in the vegetative system in the eye, influences accommodation; and this shows us why it is extremely difficult to fit glasses to patients whose nerve equilibrium is disturbed (neurasthenics). It also explains the disturbance in accommodation during toxemia, because toxemia acts upon the *sympathetic* system, and disturbs the normal equilibrium. It can be seen also how the eye symptoms are produced in exophthalmic goitre. Stimulation of the vagus increases the secretion of tears; while stimulation of the *sympathetic*, decreases it.

In the gastrointestinal tract, vagus stimulation increases appetite, increases gastric secretion, including hydrochloric acid; increases the secretion of the mucous glands of the gastro-intestinal tract and the secretion of the liver and pancreas. *Sympathetic* stimulation decreases appetite, decreases the gastric secretions, including hydrochloric acid; decreases the secretions from the mucous glands of

the intestinal tract, liver and pancreas. Vagus stimulation increases motility of the stomach and intestines. *Sympathetic* stimulation decreases motility of the stomach and intestines.

Thus we can understand the dry furred tongue, decreased digestive capacity and constipation which accompany toxemia, particularly that of the acute type such as is found in the acute infectious diseases. This is an indication of marked sympathetic stimulation. Hyperacidity, hypermotility (either gastric or intestinal), pylorospasm, and spastic colon, are all indications that the equilibrium of the vegetative nervous system has been upset and that the vagus has been the division which has been overstimulated.

In the respiratory system, *vagus* stimulation increases the irritability of the mucous membrane of the nose and throat; increases the secretion of mucus in both the nose and throat; also, produces bronchial spasm and increases bronchial secretion. *Sympathetic* stimulation decreases the secretion and irritability of the nose and throat, and decreases the bronchial secretion and relaxes bronchial spasm. Hay fever and asthma then, are both expressions of increased vagus stimulation. Both may be ameliorated or relieved by the administration of atropin, which is a direct pharmacological antagonist of the vagus, or by adrenalin which stimulates the sympathetic nerves and causes them to oppose the vagus.

In the circulatory system, conditions are different from what they are in the respiratory and digestive systems. In the respiratory and digestive systems, the *greater vagus* is the system which produces increased muscular activity, while the *sympathetic* causes muscular relaxation. In the circulatory system, however, the opposite is true. Stimulation of the *sympathetic* produces vaso-

constriction, increases the rapidity of heart action, and raises blood pressure; while the *vagus* system slows the heart's action, causes reduction of blood pressure, and in some instances apparently opposes vasoconstriction, although other factors come in here which make this phase of the subject extremely difficult to understand.

Nearly all secreting organs (suprarenals and thyroid are exceptions) have their secretory power increased by vagus stimulation, and it seems that each organ produces metabolites during its action, which act upon the arterioles and produce vasodilatation. In this way we account for the fact that each organ during activity shows a dilatation of its blood-vessels, which affords the opportunity for the increased supply of blood necessary for the extra work thrown upon it.

The innervation of the sweat-glands is as yet difficult to understand. Sweating seems to be a part of both increased sympathetic and increased vagus stimulation. Pilomotor muscles are supplied by the sympathetic system.

#### SYMPATHETIC AND GREATER VAGUS SYNDROMES.

From our discussion thus far, it will be recognized that when the tonus in either the sympathetic or *greater vagus* systems is increased, we should have more or less definite pictures. These might be spoken of as the syndrome of increased sympathetic tonus and the syndrome of increased vagus tonus.

In order to appreciate the result of excessive stimulation in either of these divisions of the vegetative system, it is necessary to fix definitely in our minds these two syndromes.

Our study of the vegetative system has been facilitated by the fact that there are certain pharmacological remedies and certain internal secre-



tions which act largely or wholly upon one or the other division. For example: Adrenin acts upon the sympathetic system; and when injected into the body, produces the same symptoms as though the sympathetic system itself were stimulated. Pylocarpin, on the other hand, produces for the most part the same group of symptoms as is caused by increased vagus stimulation. Atropin has proven to be antagonistic to the *greater vagus* although its effect is not so strong in some divisions as in others. Its action is particularly weak on the sacral branches. Ergotoxin is also used at times as a paralyzant of the sympathetic fibers.

*Sympathetic Syndrome.*—From the use of these remedies we have learned that the syndrome of predominant *sympathetic* stimulation results in some of the following symptoms: Dilatation of the pupil; pushing forward of the eyeball; decreased lacrymal secretion; decreased salivary secretion; decreased secretion of the gastric and intestinal glands, including the liver and pancreas; decrease in the secretion of the mucous membrane of the air passages, both upper and lower; relaxation of the muscles of the air passages; increased tonus of the ileocecal valve; increased rapidity of the heart's action; lengthening of the rest pause in the heart; vasoconstriction; increase of blood pressure; increase of the amount of glycogen in the blood stream; contraction of the pilomotor muscles; contraction of the muscles of the sweat glands; and an increase in the leucocytes, particularly the neutrophiles.<sup>3 4</sup>

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3. Pottenger. The Syndrome of Toxemia; An Expression of General Nervous Discharge Through the Sympathetic System. (Journal of American Medical Association, January 8, 1916.)

4. Ibid. Clinical Tuberculosis. (C. V. Mosby Co., St. Louis, 1917.)

*Greater Vagus Syndrome.*—On the other hand, the syndrome of predominant vagus stimulation consists of contraction of the pupil; contraction of the ciliary body, shortening of the focal point of the eye; increased lachrymation; increased salivary secretion; increased secretion of the glands of the gastric and intestinal tracts, including those of the liver and pancreas; increased motility of the stomach and intestines, the former leading to nausea and vomiting, the latter to spastic constipation or diarrhea, according to the degree of stimulation or according to whether the circular or longitudinal fibers are particularly irritated; spasm of the pylorus; spasm of the anal sphincter; increased irritability of the mucous membranes of the upper and lower air passages, causing sneezing and at times laryngeal spasm or bronchial spasm; increased secretion in the upper and lower air passages; slowing of the heart beat; lowering of blood pressure; decreased coagulability of the blood; vasodilatation in certain areas; a general tendency to perspiration; eosinophilia and lymphocytosis.

In these two syndromes, one will find a large number of the symptoms met with on the part of the internal viscera. Their variability depends upon the normal tonus of the *sympathetic* and *greater vagus* in each individual; also upon the fact that a person may show an increased tonus in one part of the *sympathetic* or *greater vagus* division and not in all.

CLASSIFICATION OF SOME OF THE COMMON SYMPTOMS INDICATIVE OF FUNCTIONAL DERANGEMENT.

Analysis of the above syndromes shows that in the respiratory tract, the digestive with the exception of the ileocecal valve and the internal anal sphincter; and the genito-urinary tract, increased

sympathetic stimulation produces a hypofunction, both in muscular and secretory structures. In the circulatory system, on the other hand, increased sympathetic stimulation produces a hyperfunction, giving an increased rapidity of heart beats and a general vasoconstriction, with resultant increase in blood pressure.

Increased stimulation of the *greater vagus*, on the other hand, produces a hyperfunction in the respiratory, gastro-intestinal and genito-urinary systems, increasing secretion and motility. In the circulatory system, on the other hand, it slows the heart beat, lengthens diastole and weakens the ventricular contractions; and in certain locations at least, produces vasodilatation.

If we take up some of the common symptoms and syndromes met in every day practice, we shall find that they may be analyzed according to their relationship to these two divisions of the vegetative system.

*Hay Fever*.—Hay fever shows as an increased lachrymation; increased irritability of the nasal mucous membrane, resulting in sneezing; increased secretion of the nasal mucous membrane; and sometimes both increased secretion of the bronchial mucous membrane, and bronchial spasm. Thus it can be seen that this is a definite picture of increased irritation of the respiratory and ocular branches of the greater vagus.

*Asthma*.—Asthma is a condition which is accompanied by bronchial spasm and increased bronchial secretion; sometimes an increase of secretion in the upper air passages; and a tendency to cough; and often eosinophilia. This is also indicative of increased vagus stimulation. It often occurs in patients who have other symptoms of increased vagus tonus; and may be accompanied by them, such as hyperacidity and spastic consti-

pation. The heart beat, which would naturally be slow if it showed the same increased vagus irritation, is increased in its rapidity by the dyspnea present.<sup>5</sup>

*Hyperchlorhydria.*—There are many functional disturbances on the part of the gastro-intestinal tract that can be separated according to their action upon the sympathetic and *greater vagus*. Hyperacidity must be looked upon as a functional derangement. It may result from an organic disease of the stomach itself or from any irritation which expresses itself in increased tonus of the gastric branches of the vagus. It is extremely common as a symptom of gall bladder disease and of appendicitis. It likewise comes in tuberculosis as a result of the inflammation of the lung tissue; and can be found as a result of inflammation in many of the other important internal viscera. Hyperacidity is usually accompanied by either an increased tone of the stomach wall or increased motility. It is very likely to be accompanied by some degree of increased tone in the pylorus which at times may result in definite spasm.

*Hypochlorhydria.*—Hypochlorhydria is commonly found in patients suffering from acute infectious diseases or chronic infectious diseases, during stages of acute exacerbations. The depression of gastric secretion, including hydrochloric acid, is due to the toxemia acting through the sympathetic nervous system. This accounts for the long recognized fact that hydrochloric acid is indicated in therapy in convalescence from acute infections.

*Nausea and Vomiting.*—Nausea and vomiting are also symptoms due to increased vagus tonus.

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5. Ibid. Asthma: Considered in Its Relationship to the Vegetative Nervous System. (Read before Thirty-fourth Annual Meeting of the American Climatological and Clinical Association held at Lakewood, N. J., May, 1917.)

A patient suffering from hyperchlorhydria often shows slight nausea and sometimes shows vomiting as well. These symptoms are common whenever any portion of the gastro-intestinal tract is inflamed. They frequently accompany inflammation of the gall bladder or appendix, or inflammation further down the bowel. They are also frequently present in pulmonary tuberculosis, the irritation coming from the lung and reflexly influencing the gastric muscle.

*Intestinal Stasis.*—The subject of lessened motility in the intestinal canal has received much attention during recent years, but it has been attacked too much from the standpoint of being a disease entity of itself, which it is not, except in rare cases of mechanical obstruction.

Intestinal stasis may be due to either stimulation of the sympathetics or vagus, but more often the latter. The motility of the ileocecal valve is controlled by the sympathetic nervous system. Where we have marked stimulation of the sympathetic system, as occurs in acute toxemia and in the presence of acute infectious diseases, it would be natural that there should be some interference with the ileocecal valve, retarding the emptying time of the ileum. Such conditions are also accompanied by a relaxation of the gastric and intestinal musculature and a lessening of the secretion of the gastric and intestinal mucous membranes, which would also have an influence in retarding the onward movement of the intestinal contents. The motility of the colon being also decreased by the same stimulation, the stasis of the intestinal contents is continued on throughout the entire bowel.

Ileostasis due to vagus stimulation is of another type. Moderate vagus stimulation has a tendency to increase the tone of the muscles of the intestinal tract and if it exerts itself particularly upon

the circular muscle fibers, we have a constriction which interferes with the movement of the intestinal contents, leading to the very common condition of spastic constipation.

Spastic constipation is nearly always accompanied by some degree of hyperchlorhydria. The reverse is also true. If the longitudinal fibers are overstimulated, diarrhea results.

*Bradycardia.*—Bradycardia is a symptom of increased vagus tonus. It has been noted in inflammation of the gall bladder, sometimes as a symptom of appendicitis, and also in inflammation of the stomach and intestine. We note it commonly also as a result of inflammation of pulmonary tissue. It can result wherever marked irritation of the vagus takes place, providing it expresses itself reflexly in the cardiac branch of that system.

*Disturbance in Auriculo-ventricular Conduction.*—Very often we find as a result of vagus stimulation, a disturbance in conduction of the impulse, so that the auricular contraction is not properly conducted to the ventricle. This forms a partial heart block. This is the type of irregularity that is produced by digitalis. It can be overcome by lessening the vagus irritation by the administration of atropin, or by overcoming it by stimulating the sympathetics with adrenalin.

*Tachycardia.*—Tachycardia is sometimes a symptom of direct sympathetic stimulation. This is the type that we find in the presence of acute toxemia; also that which is produced by the administration of adrenalin and by such depressive emotions as worry, fear, discontent and discouragement.

*Toxemia.*—Toxemia in its general expression is a widespread stimulation of the sympathetic nervous system, in which the system seems to be stimu-

lated in its entirety. There is a general inhibition of action on the part of the gastro-intestinal, respiratory and genito-urinary systems; increased stimulation in the circulatory system producing rapid heart action and vasoconstriction, which interferes with heat dissipation, causing rise in temperature; and increased motility in the subdermal musculature (goose flesh).

*Depressive Emotions.*—There is a group of symptoms which is generally recognized as following such emotional states as pain, fear, anger, disappointment, discontent and worry. These recently have been made the subject of careful physiological study by Cannon<sup>6</sup> and others, with the result that they are found to belong physiologically to the group which express themselves through general *sympathetic* stimulation.

In all conditions in which there is central sympathetic stimulation, there is a stimulation of the adrenal gland. The adrenin, which results from the stimulation, acts upon all structures supplied by the sympathetics, producing and prolonging the same effect.

#### REASON FOR VARIABILITY OF SYMPTOMS ON THE PART OF INTERNAL VISCERA.

One thing that we cannot fail to notice in our study of these various functional disturbances, is that the group of symptoms which is produced by stimulating certain branches of the vegetative system, are not always all present under what seem to be the same conditions. This may be due to a difference in the individual. One person has a vagus system that is more irritable than another; likewise, one has a sympathetic system which is more irritable than another. Where infection in-

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6. Cannon. Bodily Changes in Pain, Hunger, Fear and Rage. (Appleton, 1915.)

volving an important viscus is present, we now understand that expected symptoms may not appear because we have stimulation of both divisions of the vegetative at the same time. The toxemia stimulates the sympathetics, while the inflammatory process itself has a tendency to produce reflex action in other structures through the vagus. The severity of the symptoms in a given case, as well as the individual symptoms which appear, are determined by the relative strength of the stimulation through the sympathetics and the vagus. Thus, one patient with gall bladder disease will suffer severely from nausea and vomiting, while another will not; one will have marked hyperchlorhydria, and another will notice no increased acidity. The same is true of appendicitis. In our tuberculous cases we see many instances of slow heart due to the reflex stimulation from the inflammation in the lung acting upon the cardiac branch of the vagus. We often see this most marked during periods of acute inflammation in the lung when marked toxemia is present, stimulating the sympathetics and tending to produce a rapid heart. On the other hand, in other cases we see the heart assume about its normal ratio to the temperature curve, the reflex irritation of the vagus showing no signs of action <sup>4 7</sup>

With this brief analysis, I hope that I have been able to impress upon you—not only the importance of the study of visceral neurology, but also to point out some practical points which will aid in the better understanding of many of our common symptoms.

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7. Pottenger. The Relationship of Pulmonary Tuberculosis to the Vegetative Nervous System. (Read before American Medical Association Annual Meeting, held at New York, May, 1917.)