draw an analogy between the conscious and the sub-conscious, or *vice-versâ*, because they were two separate things, and not comparable with each other. Secondly, there was actual molecular shock in the shell-shock cases; and thirdly, hypo-thyroidism. Some of the brains of shell-shock cases had been examined, and the changes found in the nervous system were remarkable.

He commended to members the researches of Cannon in the Harvard University. He put cats into cages, and got dogs to bark at and worry them; then he examined the blood, and found the adrenals increased their secretion; the blood-pressure went up, glycogen was released, and in that way energy was supplied to the muscles ready for waging the imminent combat. One might ask why, with that view, one found a man who had great fear was collapsed. It was necessary to carry the point a little further. When injuries had been received through fear, it became evident that it was not to the advantage of the organism to show combat, the only advantage was to show concealment, and so the organism collapsed, and at that time adrenalism had had its innings. Dr. William Brown had shown that in fright the pressure of the blood and the pulse-rate came down. He had been asked by Major Newton Pitt to see a case in which goitre had developed, and Dr. Helen Boyle's experience supported the view that goitre might occur almost spontaneously, in which case one found hyper-thyroidism. He would like to know whether Dr. Springthorpe would regard fright as the cause of the adrenalism. There was a case of an officer, now in Queen Alexandra Hospital, who was seventeen months in the trenches. Then he was shot in the thigh, and had been in bed seven months, and had undergone nine operations. Though he had been a brave commanding officer, he now wept like a baby, declaring he could not help it. He had never previously felt fear, and the speaker thought the best explanation was that the nerve potential had gone down, the battery was now exhausted. That seemed to be the condition of many of these cases.

Dr. Helen Boyle succeeded in burying painful things. She was, he considered, a super-optimist. He (Sir Robert) had never succeeded in doing so, hence the question of temperament came in. He felt he had a right to speak of Dr. Boyle in the way he did, because he had the privilege of working with her at Claybury Asylum for five years.

In conclusion, Sir Robert expressed the thanks and gratitude which he felt on hearing the President's cordial reference to the honour which had been conferred upon him. He had very warm feelings towards the Association, with which he had been so long connected, and which contained so many of his friends. And the honour was not simply a personal recognition of himself, but of those with whom he had so cordially worked.

Remarks upon the Vegetative Nervous System and the Internal Secretions.(1)

By FREDERIC J. FARNELL, M.D., Butler Hospital, Providence, R.I.

IT will not be my desire to enter upon a full discussion of internal secretions; still it will be touched upon sufficiently in an attempt to link some disorders of nervous origin with a condition clearly defined by Eppinger and Hess as vagotonia.

As in all other special fields of medicine nervous and mental traits follow certain tendencies among certain types of people, or even among certain communities, and these tendencies are usually shaped by causes more or less inherent for those people; of this all are aware. That there is plenty of clinical

https://doi.org/10.1192/bjp.63.261.225 Published online by Cambridge University Press

evidence to warrant such a justification has been pointed out, as a factor in mental disorders, by Meyer, Hoch, and others, who have clearly defined types of personality as quite characteristic in certain mental disturbances.

When one considers the cause of a nervous disorder one must distinguish the case of a person in the best of health suddenly developing a nervous disturbance from one in which a lingering constitutional weakness becomes exaggerated by an intercurrent affection. It is to these tendencies which deal with the fundamental ætiological relationship of a great majority of nervous states that these remarks will refer.

One cannot help while reviewing the study of vagotonia but recognise Sir Grainger Stewart's classification of constitutions and diathesis as falling closely within the group of so-called vagotonics. His classification was somewhat as follows:

(1) *A nervous constitution*, generally with a fair complexion, bright eyes, frequent changes in colour and facial expression, bones and muscles not strong or vigorous, the heart and nerves excitable and unstable.

(2) *The lymphatic constitution*, with great head, irregular fleshy face, slow weak pulse, large hands and feet, and so forth.

(3) *The sanguine constitution*, fair hair, blue eyes, easily flushing face, strong but excitable heart, yet no nervous states.

(4) *The bilious constitution*, with a tendency to obesity, dyspepsia, variable intestinal phenomena, usually diarrhœa, urinary disorders, etc.

How often one comes across a mixture of "lymphatic," "nervous," and "bilious" constitutions, yielding very plainly the "vagotonic disposition" as described by Eppinger and Hess. These people appear for advice because of some rather slight ailment, "indigestion," "constipation," or a fear that high blood-pressure is making itself manifest. They might enumerate many symptoms heretofore called "neurasthenic," and they are looked upon as individuals with nerves, and little attention is paid to them.

Their symptoms are usually spasmodic and episodic. Their faces flush easily, and one often hears them refer to the periods of paleness and blotchiness of their face and neck. Their extremities become cyanotic, with palmar sweating, and occa-

sional complaints of regional areas of sweating. They complain of eructations of gas, regurgitation of food, and a tendency to vomit. Bloating and "a feeling of pressure" are of frequent occurrence. There is intestinal fermentation, rectal pressure and deficient bowel movement. This, through absorption of cleavage products in intestines, causes headaches, feelings of pressure, insomnia, and vertigo. Gross circulatory manifestations appear such as cardiac palpation, intermittent irregular pulse, variations in blood pressure, pulsations of the abdominal vessels.

The emotional life of these individuals is a most important factor in enhancing visceral symptoms, and undoubtedly has led many investigators to lay emphasis on the mental state, such as Freud in his "anxiety neuroses" and others. These patients have a weak affective tone, and do not respond or adjust themselves to the difficulties of everyday life. When these unavoidable experiences occur one must expect a profound visceral reaction, the type depending upon the system least sensitised. That these individuals do not wish to be called "nervous" all are aware, for it is an insult to their pride, and carries with it an assumption of "mental weakness." They carry the old idea that with mental and nervous disturbances the imagination is warped, and since the distress and disturbance are real to them their disorder must be organic and non-nervous. Whether a pain is imaginary or real it matters not, for both must be handled carefully. What the layman calls "nervousness" is often only a slight excess of normal, and very far from the state of pathological nervousness. There can be little doubt but that what has been termed "neurasthenia" has now fallen into the same category as "uric acid diathesis," blood-pressure disease, auto-intoxication, all having become obsolete, and it now behoves the clinician to dig deeper in search for causes and mechanisms.

It might be advisable at this point to refer briefly to the visceral nervous system. Eppinger has called that system which supplies the smooth muscles, cardiac muscle, and glandular tissues the vegetative system, because through it the normal continuation of life and the vital functions are preserved. The "sympathetic nervous system" is that portion of the vegetative system represented by the gangliated cord on either side of the spinal column, with its ganglia and communi-

cating fibres, which might be termed the "thoracic autonomic." The vegetative proper is divided into midbrain, whose segments pass by way of the oculomotor nerve pathways; the bulbar which through the facial, glossopharyngeal, and vagus supplies the glands, vaso-dilators of the head, heart, bronchi, œsophagus, stomach, intestines, and pancreas; and the sacral which supplies the descending colon, sigmoid, bladder, and genitals.

Concerning these different divisions, the mid-brain, bulbar, and sacral are similar in that they are entirely local in their supply; whereas the sympathetic or "thoracic autonomic" not only has its local distribution, but also it sends segments to the same structures as the other system, thus causing the vegetative system to be innervated by both autonomic and sympathetic fibres, and the sympathetic or thoracic autonomic is innervated by only one system. This is of great importance in differentiating disorders, and will be referred to in relations to glandular upsets. As examples of autonomic structure having a double supply one may mention the salivary glands, stomach glands, intestinal muscle-coats, heart, and blood-vessels. Those having a single or sympathetic, smooth muscle of skin, blood-vessels of intestines, and internal generative organs. As an example of the antagonistic action of the two systems one may instance the external genitals. As an example of double innervation of similar stimulating effect, the salivary glands, in those nerves having a vegetative activity the efferent and afferent fibres are interrupted in their course from the cortico-spinal system by preganglionic and postganglionic segments, with a variation in location from the sympathetic cord to the submucosa of the intestines. This latter nerve supply has been called by Langley the "enteric nervous" system governing the entire tract from the esophagus to the rectum. He mentions the fact that the character of their connections to the autonomic system and their control of the gastro-enteric tract is little known, but that they seem to have an action independent of the central nervous system. This has been proven by Cannon in his experiments, and he concludes that when this canal is entirely separated from the central nervous system it has a remarkable power of developing an independent tonic state, that is, it soon recovers its tone. This shows that it supplies the resiliency that causes the state of tension when the canal was filled. This tension is the occasion for the contraction of

viscera which are walled with smooth muscle holding a nerve plexus. That this tonicity is fundamental is accounted for in the failure of efferent motility in atonic states. It is an observation that tonic contraction and rhythmic peristalsis disappear in asthenia and exhaustive states. It agrees with these observations that anxiety, morbid fear, worry, mental distress, and kindred disorders stop gastro-enteric movements and abolish the tonus of the alimentary canal.

There is considerable difference of opinion as to the make up of the afferent nerves of the vegetative system. Some investigators believe the afferent nerves contain somatic fibres, and yet, if so, why should there be a difference in their functional activity? It is well known that when pain is experienced in the viscera it is usually due to a mechanical cause, and its action upon the body is, as Head terms it, reflex. This has been shown by Sherrington to be due to an elevation in the threshold of the excitability of the arc in the viscera. This difference is also extended centrally in that autonomic afferent fibres have no central connection, whereas somatic fibres have a connection in the brain cortex. Crile has attempted to disconnect this somatic system from the brain cortex by the application of what he calls the "principle of anoci-association," and believes that by so doing he has lessened his post-operative mortality.

Notwithstanding the fact that there is no evident connection between the autonomic system and the brain cortex, there must be some interrelation somewhere. The functions of the sweat-glands, the gastro-intestinal tract, and the blood-vessels are probably not in direct relation to the brain cortex, yet there is no doubt but that they are under the influence of the emotions, and through the sympathetic system. Anger, fear, and shame are expressed by pallor, blushing, sweating, and crying. These impulses must pass by the basal ganglia. Lesions of the caudate and lenticular nuclei, as seen in sclerosis of the basal ganglia and in lenticular degeneration, cause as the most prominent symptoms emotional variations, and in several cases reported (Mills, Oppenheim, Farnell), the cerebral lesions were confined to these ganglia.

It would seem only proper at this moment to refer briefly to the anxiety neuroses. Freud, in his monograph upon the psychoneuroses, states in relation to the merging of the nervous

symptoms into the peculiar affective state of anxiety having as its cause psychic inadequacy for the subjugation of sexual excitement, that the psyche merges into the affect of fear when it perceives itself unable to adjust an externally approaching danger, while it merges into a neurosis of anxiety when it finds itself unable to equalise the endogenously originated sexual excitement. The psyche therefore behaves by, as it were, projecting this excitement externally. The affect and the neurosis corresponding to it stand in close relationship to each other. The first is in relation to an exogenous, and the latter in relation to an analogous endogenous excitement. The affect is a rapidly passing state; the neurosis is chronic because the exogenous excitement acts like a stroke happening but once, while the endogenous acts like a constant force. The nervous system reacts in the neurosis against an inner source of excitement just as it does in the corresponding affect against an analogous external one. The many variations in the form of anxiety as it affects the body viscera are quite a constant and important factor in these neuroses, and it might not be inadvisable to divide this disorder into two groups, the one in which the anxiety neurosis portrays as its dominant factor psychical excitement, and the other the form in which the visceral disorders predominate. In the former the symptoms are relieved by psychological analysis, there being little disturbance in the vegetative system proper, whereas in the latter one might place the primary cause as a constitutional disposition to vagotonia, and consider that consciousness or unconsciousness produce their effect by the inherent weakness of that system. May this not be one of the reasons why Freud's theory has not been fully accepted, and in these latter types pharmaceutical preparations have produced the required results?

In the old disorder grouped as hypochondria and the condition known as cenæsthesia, both being examples of states in which consciousness is acquainted with the harmonious action of the various visceral organs, it might be difficult to decide the exact relation of the disorder to the vegetative nervous system, but there are sufficient reasons to believe that the path of psychic attention passes through the sympathetic system.

The exact location of these higher brain centres is still a matter of dispute, and yet there is evidence that it has a close connection with the chromaffin system.

The most essential parts of the chromaffin system are the nervous or posterior lobe of the hypophysis, the sympathetic ganglia and paraganglia of Kahn, and the nervous elements in the adrenals. This specialised nervous tissue has also been found embedded in the kidney, and even carried down with the ovaries and testicles in their development and descent.

Functionally this system produces in the granules of these cells adrenalin. Exception has been taken to recognising the adrenals as internal secretory organs because (Kahn) the chromaffin cells do not conform to the type of epithelial cells nor their grouping to glandular structure, yet from a physiological viewpoint the internal secretory conclusion is justified. What can be the significance of this intimate association between the glandular and nervous elements?

The production of adrenalin in these cells is now an undisputed fact. It enters the blood-stream *viâ* the vein directly. This product acts upon certain tissues, and increases the activity of metabolism. These certain tissues upon which adrenalin acts are those which possess only a sympathetic innervation with the point of election a portion of the cell in the neighbourhood of the nerve-ending, although it is generally recognised as having its action upon the nerve-ending.

One must not conclude from these remarks that this is the only function of adrenalin. The tone of the sympathetic nervous system bears a close relation to the tension of the muscle-coats of the heart and vessels, and it has its influence upon the body metabolism, especially in relation to carbohydrates, as well as metabolic processes modifying the albumin and salt-content in the blood.

An important action to be kept in mind regarding adrenalin is that where the nerve influenced is one of stimulation the adrenalin acts as one of stimulation, and where one of inhibition it is inhibitory in action. As an example of the inhibitory effect of adrenalin upon a process of metabolism undoubtedly taking place through the vegetative nervous system is its influence upon the pancreas and the pancreatic secretions. This glandular physiological relationship shows itself in other glandular derangements. Eppinger and Falta have concluded that the adrenal system plus the thyroid act as a balancing mechanism to the antagonistic activity of the pancreas and parathyroids. And yet the thyroid promotes and probably

acts as a regulator of the adrenal system. If adrenalin limits the internal secretory function of the pancreas and one stimulates the autonomic nerve (the vagus), one would expect to reach at some point a balance and adjust the disturbance. Such has turned out not to be the case, as it is now proven that stimulation of the sympathetic far outweighs that of the autonomic. This naturally would cause one to consider the action of the remaining glands of this system, the thyroid and parathyroid. The thyroid working in conjunction with the adrenals would increase the pancreatic disability, but it must be remembered that the thyroid serves a double function, being furnished with both bulbo-autonomic and sympathetic nerves. Having created a disturbance of metabolism in one organ (gland) of sympathetic innervation, one might expect the sympathetic stimulation of another gland (the thyroid). Notwithstanding these deepening suppositions one must look upon the thyroid as a "pace-maker," and hence its double innervation as a means of protection, and one frequently called into play, due to the fact that it contains probably two internal secretory mechanisms.

To illustrate these inter-reactions and decidedly complicated mechanism a case will be cited briefly.

H. C—, a boy, æt. 15, whose family present little of pathological importance except that a brother is a cretin. The patient was born at full term, labour was difficult, and delivery instrumental. He was recognised as a fine baby and weighed 12 lb. There was nothing abnormal noticed about him; he walked at 14 months, and began to talk at about same time. He had no convulsions in infancy. He appeared to develop normally until 4 years of age, when he suddenly stopped growing, physically and mentally. He did not grow fat. He would not play, was cranky and irritable as well as stubborn; wanted to be by himself. Complained of headaches and something (a numbness) in his legs. He wet the bed regularly. He was sick in his stomach, bowels were always costive requiring stiff cathartics. He talked in his sleep, and had night-mare. Had dreamy spells in which he rolled his eyes, and looked dopy in the morning. At the age of 5 years he was diagnosed as a case of cretinism. He was placed on thyroid gland but immediately, even in small doses, it caused sickness, nausea, general uneasiness, and flushing of face. The drug was therefore only given at intervals. The next five

https://doi.org/10.1192/bjp.63.261.225 Published online by Cambridge University Press

years showed extremely slow development. When seen four and a half years ago by the writer he was in much the same condition as described, and was thought to be a case of pancreatic infantilism, as described by Herter, although the stools were negative. At all events he was given 15 gr. of pancreatin three times a day, and soon showed a clearing of symptoms; his gastro-enteric system improved, he ceased wetting the bed, and he soon gained 15 lb. in weight. He continued to improve in appearance, his conduct was better, he played and entered into boyish pranks, but made slow progress in school. About half a year ago he developed terrific frontal headaches, periodical blanching, and pallor of the skin of face, syncopal attacks with evidence of poor peripheral circulation, weakness, and great fatigue. There was practically no disorder of gastro-intestinal tract. His pulse was 60, compressible, of low tension, and irregular. Blood-pressure was 65. His skin was rough and dry and pigmented. X-ray of skull showed normal sella turcica, while that of chest evinced a very small heart and a shadow over the region of the thymus. His height was 3 ft. 7½ in. and weight 69 lb. Are we not now dealing with an adrenal disorder? Is it possible that we are dealing with the condition of status lymphaticus in which the inter-activities of the chromaffin system have laid bare their individual symptom complex? Therapeutic measures have adjusted the troublesome symptoms, and for four months the patient has taken in addition to pancreatin 3 gr. of suprarenal extract, and his cardio-vascular disturbance has been relieved. His headaches ceased. His blood-pressure rose 15 mm. He has grown 1½ in. Where a year ago his testes were undescended they are now in the scrotum.

It is noteworthy that in the out-cropping of symptom-complexes in this case there was throughout an inhibition of the sympathetic, and no definite stimulation of the autonomic.

This is quite contrary to some observers who have noted symptoms of vagotonia in lymphatism due to the inferiority of the adrenal system.

To a much less degree than the foregoing one sees frequently cases of apparent hypoplasias of the lymphatic system developing at an early age epileptoid states, and presenting isolated symptoms of vagotonia. It has been a custom at our school clinic to place such children upon thyroid and pancreatin.

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Results have been forthcoming in many cases. Calcium metabolism in relation to epilepsy and its allied states has been a source of investigation for some time past. Its relation to tetany and tetanoid convulsions is now fully accepted, as well as being a parathyroid disorder. The parathyroids are antagonistic in their action to the thyroid. Thyroid and pancreatin feeding evidently does something. It cannot be doubted that it is a probable occurrence for an organ to send out chemical stimuli causing stimulation in one case and inhibition in another. The end results will also differ probably by influencing the internal secretion of another organ.

Healey and Anderson, as well as the writer, have observed in juvenile court cases the existence of status lymphaticus, a constitutional inferiority with an accompanying mental inferiority. How many of these abnormal or antisocial traits may bear close relation to internal secretory disorders is difficult to say; such as stealing money to buy sweets indicating a high sugar tolerance?

The next group of disorders, also polyglandular in type, evince a mechanism passing through both the sympathetic and autonomic nervous systems. This disturbance is hyper-thyroidism, which probably includes not only the thyroid itself but also the ovary or testes and the pituitary body. It should be again noted that both nervous systems were mentioned as being involved. Allow me to repeat a statement made previously in reference to the chromaffin system, "this specialised tissue has even been carried down with the ovaries or the testes in their development and descent." Is it possible that in those individuals who develop hyper-thyroidism, with complete disorganisation of the interactivities of that glandular chain, there is this specialised tissue in the generative organs also? This fact might be cleared up by the histo-pathologist. Or, is it a disorder passing wholly through the nervous mechanism. It is such problems as these that may lead one towards the recognition of a chemical or bio-chemical basis for nerve excitation, as well as, or in addition to, the present recognition of a physical basis.

Hyper-thyroidism is a symptom of hypersensibility of the sympathetic system or an irritability of the autonomic system. It seems difficult to attribute all the symptoms one sees in hyper-thyroidism to one ætiological cause. From the view point

that the function of the nervous system is for the control and co-ordination of the many and various body activities, one may accept the statement that there may be conditions under which this nervous system can stimulate one or more activities to excess at or about the same time. The question will then arise as to whether these pathological conditions do not arise from the interaction of causes representing the want of a balance between an excessive amount of material thrown out and a lesser amount of material upon which to act.

That the clinical picture of hyper-thyroidism may vary greatly during the course of the disease process seems to bear out the statements just enumerated to a fair degree. For example, a female, æt. 37, single, whose family history was negative. Her previous history presented nothing remarkable except that she was always active, happy, not easily upset, had plenty of friends, home conditions the best, etc. The symptom-complex as presented upon the initial examination was as follows: moderate exophthalmus, von Grafe's sign marked, profuse perspiration, flushing of the face, cardiac palpitation, increase in gastric acidity, dyspnœa. These symptoms are what Eppinger and Hess group under the heading of vagotonic. At the end of a few weeks of treatment many of these symptoms were relieved, but there developed a very marked degree of tachycardia, her hair fell out in large quantities, and in the course of time she had several attacks of fever. Notwithstanding these symptoms there was progressive gain in strength and weight. Eppinger and Hess place elevation of temperature in the group of sympathicotonias. Can this be rather an attempt at harmonising antagonistic activities which bear a close relation to the functioning of the tissue; a central control, through the sympathetic system, maybe, rather than an irritability of the sympathetic occasioned by the thyroid secretion?

Some investigators have attempted to show that the symptom-complexes of hyper-thyroidism are constantly parallel in all stages of development and regression, with similar stages in development and regression in the secreting cells of the gland; the hyperactivity being due to a toxic compound containing 60 *per cent.* iodine which is attached in either an alpha or beta position, the former being toxic and the latter non-toxic. From glands removed during the various stages of the

https://doi.org/10.1192/bjp.63.261.225 Published online by Cambridge University Press

disease the amount of iodine obtained varied with the stage from a little less than normal to 1 in 20, or 1 in 15 less than normal. This cannot be interpreted as a reduced production (iodine compounds (KI) have caused symptoms of hyperthyroidism) but as a greatly increased effusion of the substance into the blood stream. Therefore the clinical picture would vary according to the amount given out, the length of time during which the intoxication occurred, and the constitution of the patient.

If one goes a little further and divides the course of the disease into three stages (for one is bound to meet cases in various stages, or even in a mixture of stages), (1) the stage of autonomic irritability, (2) the stages of sympathetic irritability, (3) the effects of a disordered vegetative function, it is the writer's feeling that both Eppinger and Hess's and Wilson and Kendell's versions can be accepted. Eppinger and Hess have noted clinical cases which they have termed "Basedowoid conditions, which have yielded quickly to atropine. These cases might have been merely "vagotonics." Kendell has grouped these cases as "non-hyperplastic toxic goitres," a condition in which the iodine content is diffused in a lessened amount.

This shows to better advantage in typical Graves' disease, a disorder which reacts poorly to atropine in many cases, especially so when the tachycardia and the increased metabolic changes are taking place. It is these cases, termed by the Mayo Clinic as "hyperplastic toxic goitres," that the diffusibility of the iodine is at its greatest, and which, in the writer's small series of cases, have reacted quickly to cytotoxic serum, an antiserum low in the iodine content. Experiments have shown conclusively that iodothyroidin and atropine are not antagonistic.

The third division is that series of cases which have been relieved (through rest, bromides, *etc.*) of those symptoms of vegetative irritability, and show secondary glandular disorders with slow, but gradual, metabolic changes. It has been the custom to feed these patients with nucleo-proteid and adrenal gland with good results.

Falta and Eppinger assume a polyvalency of the thyroid secretion, and regard typical Graves' disease as an outcome of a simultaneous, though probably independent, stimulation of both the sympathetic and autonomic nervous systems. Biedel,

however, suggests that this secretion might be due to a primary affection of the sympathetic nerve, or the nervous areas in which it takes its origin.

This brings us back to the exciting factor in this neurogenic hypothesis; most writers place emotional disturbances first, and many cases might be cited in which emotion was at the root of this disorder, again evincing a connection with higher nerve centres.

In line with these conceptions attempts have been made to connect certain mental states and psychic disorders with over-irritability of the vegetative nervous system. Such a connection has been assumed to exist in depressive states at puberty and the menopause, in traumatic neuroses, in the self-accusatory and depreciative types of dementia præcox. As all are aware, these disorders are maladjustments towards the environment—worry, which is a conflict between hope and fear, conduct disorders, sexual or what not, religious or ethical problems. Sherrington has said: "Evironment drives the brain, and the brain drives the various organs of the body." Can it not be that this system, the vegetative nervous system, plays a most important part in adjustment, and acts as the most essential stimulator into action? Attached to this reactibility is its power to influence and direct functional conditions, not evident under ordinary conditions, but aroused when given the chance —constitutional tendencies, disorders of personality, susceptibility.

To quote from Hibbin: "Synoptic man is one who sees the verities of life in their true relations, properly co-ordinated and sub-ordinated, and who in particular pursuits, however absorbing, does not ignore the unity of the whole, nor overlook the universal aspect of even the commonplaces of life."

(1) Presented before Boston Society of Neurology and Psychiatry, March 20th, 1916.