A Lecture

ON

VASOVAGAL SYNCOPE AND THE CAROTID SINUS MECHANISM

WITH COMMENTS ON GOWERS'S AND NOTHNAGEL'S SYNDROME

BY

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In the present article a form of fainting is described for which the term "vasovagal syncope" will be found most appropriate. It forms a common and interesting disturbance of a transient kind. It will be described and discussed in relation to a mechanism that has been under close investigation in recent years. There is another and distinct condition with which terminology tends to confuse it—namely, what I shall call for convenience "Gowers's syndrome"; there is also a third condition, probably comprising a vasomotor disturbance—namely, "Nothnagel's syndrome," and thought by some to be identical with Gowers's syndrome. The available evidence relating to these last two maladies will be considered sufficiently to allow us to see what there is in it of significance from the standpoint of the vascular system.

VASOVAGAL SYNCOPE

Thirteen years ago I[1] became interested in what may be called common fainting attacks, or, more precisely, vasovagal syncope. Such attacks had long been known, but although many essays were written in the eighteenth and nineteenth centuries upon syncope, actually it was not until the analysis of disordered action of the heart beat was accomplished that a real basis for differentiating between forms of syncope, trivial and grave, was found. I have previously indicated the belief that that very active phase of clinical work, during which cardiac irregularities were sorted out, meant far more to medical progress than the mere analysis of disordered action of the heart beat. It brought with it a sharpened and more rigid point of view, clear recognition that much of what had stood for knowledge in medicine was hypothesis based on slender foundations, and a more insistent demand that reasoning from ascertained facts should replace speculation. Syncope may be used as an illustration of this changed outlook. Graphic methods of studying the heart's mechanism soon enabled types of syncope, due to disordered action of the heart, to be divided off, and, because these became well defined in the process, they were divided off with finality. Other and commoner types were for the moment left where they were, but not without its becoming manifest by contrast that their nature was almost unknown. Although the form of syncope of which I shall speak was widely regarded as a thing apart, it had received no analysis. The very simplest facts necessary to its isolation and description, such facts as the change in pulse rate and in blood pressure, were practically unknown, and precisely for this reason it remained undefined and its clinical associations could not be recognized. It became obvious that if progress were to be made it would be necessary to witness these fainting attacks and to make deliberate observations during them. This was done in a number of subjects by Cotton and myself. These seem to have been the first precise observations of the kind to be recorded, and appear not to have been added to materially by other workers. Since our original report similar observations have been made in my department, and with the help of these I am able to speak more fully of the types of patient in which the attacks occur.

We studied the attacks first of all where we had unusual opportunities—namely, in young soldiers invalided to our war hospital in large numbers for a condition since termed "effort syndrome," a state of ill-health in which the normal response to exercise is exaggerated. The fact that we studied the phenomena in these subjects was a matter of little consequence, and should not be regarded as meaning that the attacks are peculiar to these clinical cases. Any such study must of necessity start with a given clinical type, to safeguard, as far as possible, against confusing attacks of different kinds; and the investigation must first establish by analysis, and thus define, a type of seizure. Time enough when that is done to search more widely to ascertain the full clinical associations. The present purposes of this lecture are to re-describe the common type of syncopal attack in such a way that it may be clear as an entity and that its recognition may be facilitated or assured, and to put forward certain ideas relative to its pathology.

I will deal first, but only briefly, with the clinical associations. Actually this field is still largely unexplored, a fact which provides a motive in bringing the clinical associations momentarily into the foreground.

Although we described our type of syncope in young soldiers in ill-health, we recognized then, and have recognized increasingly since, that its incidence is wide. It is, in fact, the commonest form of syncope or fainting. It occurs in both sexes; it affects the young especially, but by no means exclusively. There are states of the body that can be named as predisposing to it. Thus it is more usual in people who are out of condition or actually in poor health; it is more frequent after an illness or chronic infection. The presence of fatigue, a period of fasting, confinement to an overheated, overcrowded room, are not unusual attendant circumstances. These examples, which will at once recall instances within the experience of most medical men, belong to the type under consideration. It is important to say that this statement is based upon the knowledge that the characteristic manifestations presently to be described are actually displayed in these instances. On similar grounds I can state that the same attacks occur in cases of chronic heart disease, including aortic regurgitation. It is of consequence that this should be recognized, for syncopal attacks in such an association give rise to an alarm that is often unnecessary. We are perhaps too apt as medical men to ascribe all symptoms arising during the course of a major disease to that disease, and too disinclined to realize that transient disturbances, which not uncommonly yield symptoms in relatively healthy folk, also occur in cardiac patients. But the attacks are not confined to people who are unwell or who are under trying conditions of physical environment; they occur also in people in apparently robust health. Frequently the stimulus provoking the attack can be named; it can usually be named when the subject is robust. Nervous agitation and emotional stress, especially if suddenly developed, are commonly provocative—for example, an abrupt order or threat, an unexpected and important encounter, the receipt of unusual and stirring news, or the witnessing of a distressing accident. In healthy people, completely at ease, the provocation may be adequate without arousing feelings either of disgust or dread. In these instances there is usually an element of surprise, as when a subject sees blood flow into a syringe from his own arm, the arm redden in reactive hyperaemia, or a sphygmograph lever begin to move on his own wrist.

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Of syncope, occurring as it is well known it may in response to pain, I speak a little more diffidently, but I have strong reason to suspect that syncope during the painful phase of coronary thrombosis, during the manipulation of disused joints, in gall-stone colic, and in renal colic, is of the kind discussed ; but, in the case of most of these, sufficient observations have not been made as yet positively to identify the form of syncope ; they should be made, and that is chiefly why I am instancing them.

PHENOMENA OF THE ATTACK

The description of the attacks may begin with an actual example ; others will be found in our original report.

A soldier, aged 21, was invalided from active service. From his schooldays until the time when he was seen he had been unable to play strenuous games owing to breathlessness and the early onset of exhaustion. He was invalided for these symptoms and because he had fainted while on guard duty when attempting to salute an officer of high rank of whom he became aware abruptly. He was an undersized and poorly developed man, presenting no clear signs of disease in heart or other organs. On December 18th, 1916, the patient was sitting, and a few cubic centimetres of blood had been withdrawn from a vein in the arm and the needle removed. He was watching the operation and began to feel queer, "as though his stomach had turned upside down" ; he complained of dizziness, facial pallor was noticed, and his head fell forward to his knees. He was placed at once in a long easy-chair and further observed. By this time the pallor was intense and he was restless. The pulse was imperceptible ; the heart sounds distant, its rate of beating being 50 per minute ; the action was for the most part regular, a single premature beat being noticed. From time to time there were retching movements. The pupils were little, if at all, dilated. The patient was limp, mentally confused, or actually unconscious, for several minutes ; a heavy sweat broke out over his forehead, spreading over chest and body ; the pallor remained extreme. Respiration was slow and sighing. The pulse was imperceptible for several minutes ; as it returned, the systolic blood pressure was registered at 60 mm. ; a little later the pressure fell to 55, then to 50 ; the pulse rate varied between 50 and 60. Five minutes after the onset some recovery was observed ; the pulse rate had risen to 64 and the blood pressure to 80. Nine minutes after the onset the patient was able to respond to questions. The pulse rate was 88 and the blood pressure 105 ; the blood pressure gradually rose to 110. Half an hour later he was able to leave the chair and walk unsupported across the room. He was tremulous and tired for thirty-six hours subsequently. His average blood pressure in ordinary circumstances was 118 and the pulse rate 80 to 90.

To generalize, the central feature of the attack is the syncope. In some cases the loss of consciousness occurs without warning of any kind, and may then result in a heavy fall and injury. More usually the subject is aware that fainting is imminent and sits or lies down deliberately, or slips, or falls more slowly and involuntarily to the ground. The warning consists of a feeling of instability or uncertainty, a dimming of vision, and a feeling of giddiness. There is never any sense of rotation or of objects swinging around before the eyes, often a very valuable point in differentiating auditory vertigo. The attack occurs rarely, if ever, while the subject is lying down, a point that in the history is often crucial in differentiating the attack from major attacks of cardiac syncope or epilepsy. The standing or sitting position is the rule. (There is another and frequent form of giddiness, occasionally leading up to syncope, which is due to a distinct mechanism ; it is characteristic of this giddiness that it is usually related to the act of rising to the erect position.) In the syncope here described there may be at an early stage a peculiar feeling in the abdomen, sometimes described as like that experienced in falling rapidly in a lift, or in association with nervousness ; it is generally accompanied by nausea, sometimes by retching, sometimes by the feeling that the bowels will be moved shortly.

In uncomplicated cases I have not known patients to speak of precordial distress or constriction, or of any real alarm. The symptoms that have been discussed all belong to the attack ; to describe them as premonitory is merely to say that they occur before consciousness is actually lost ; the cardiovascular changes leading up to loss of consciousness have already begun. From the start there is a progressive lowering of blood pressure and almost always a steep fall of heart rate, the pulse usually becoming imperceptible and the heart rate falling to 50 or 40 (unusually to 30 or 20) beats per minute. Pallor accompanies this fall of blood pressure ; increasing in intensity, it ultimately becomes extreme in the face, but is absent or much less evident in dependent parts, such as the hands. This pallor is of the type associated with simple drainage of blood from the skin to dilating visceral vessels. The cerebral manifestations indicate the degree and duration of cerebral anaemia, and from the standpoint of the circulation are to be regarded as incidental. When the circulatory changes happen gradually, syncope is led up to by feelings of insecurity and dimness of vision, objectively by incoordination, confusion of speech, restlessness, yawning, and decreasing response to questions and to physical stimuli ; actual loss of consciousness with flaccidity is the rule. If the changes are sufficiently profound the pupils dilate and the conjunctival reflex vanishes ; there may be slight clonic movements of the face, upper limb, and trunk. The tongue is not bitten, nor is the urine passed. In the severer attack, respirations are slow, deep, and sighing ; sweating is almost invariable, breaking out on lips and forehead, or over the body generally ; usually free, it sometimes drenches the clothing.

Recovery is invariable, and is generally slower than is the onset ; in it the patient is limp and inert, and the skin is pale and wet. The attack is almost always brief, lasting usually from two to ten minutes, occasionally longer ; it leaves the patient tremulous, weak, and sometimes with severe headache ; these after-effects are usually brief, but may last for hours. A large quantity of watery urine if often passed after the attack.

CAUSE OF THE SYNCOPE

The slow pulse in the attack is due, as has been shown polygraphically, to a slowing of the whole heart ; irregularity, a common feature of vagal slowing, is often displayed. The proof that slowing is vagal is given by atropine, which promptly drives the rate to levels usual under atropine.

The slowing of the heart to 50 or 40, exceptionally to 30 beats per minute, is insufficient to induce unconsciousness ; such rates are frequently seen in cases of heart-block that are without symptoms. The idea that, because the vagus is responsible for the slowing, the force of ventricular contractions will be weakened, is open to serious doubt. Appreciable weakening of the beats from this cause has not been demonstrated in mammals ; in the dog the heart rate may be reduced to one-half by vagal stimulation without altering the mean blood pressure materially. Undoubtedly the main cause of the fall of blood pressure in these attacks, and the enfeeblement or loss of pulse, is independent of the vagus, and lies in the blood vessels. Atropine, while raising the pulse rate up to and beyond normal levels during the attack, leaves the blood pressure below normal and the patient still pale and not fully conscious. Attacks in which the blood pressure sinks without a lowering of pulse rate, and the patient verges on unconsciousness whenever the pressure reaches certain low levels, have been encountered. Thus,

the cause of syncope is mainly vasomotor and not vagal ;* but the vagus adds impressively to the clinical picture by inducing conspicuous slowing of the heart and gastric manifestations. The combination of vagal and vasomotor effects, while fully justifying the term "vasovagal," brings me to the consideration of a discovery which is possibly very relevant to the pathology of the attacks now discussed.

CAROTID SINUS REFLEX

In recent years a very great deal of interest has been aroused in a mechanism connected with what is now called the sinus caroticus. This mechanism has been shown to exercise a powerful controlling influence upon heart rate, blood pressure, and respiration, and especially in regulating the circulation to the brain. A rise of pressure within the carotid sinus results in a reflex lowering of heart rate and of systemic pressure ; the former is produced through the vagus, and the latter through vasomotor nervous channels (Hering)[2] and through an effect on suprarenal secretion (Heymans).[3]

This important discovery has come to us originally, as so many have, through clinical observations. Hering is, in the true sense of the word, the discoverer, in that his careful and prolonged researches first gave proof that a special mechanism exists, and located it. Hering was led to this investigation during the period when he was carrying out his important clinical observations upon patients suffering from irregularity of the heart. He was struck by the lightness of pressure upon the carotid sheath, near the bifurcation of the artery, that sometimes suffices to produce slowing of the heart rate, and it seemed to him improbable that the latter could result from stimulation of the vagus. The fact that pressure upon the carotid region of the neck will slow the heart had, of course, been known for many years previously, and such pressure has often been referred to, though incorrectly, as Czermak's experiment.[4] This physiologist published his observation upon pulse-slowing in 1866 ; both he and Waller,[5] whose publication came four years earlier, attributed the effect to stimulation of the vagus nerve. But the original observation is neither Waller's nor Czermak's ; it is Parry's. This Welshman, famous as clinician and experimenter, wrote in 1799[6] as follows:

"In patients whose hearts have been beating with undue quickness and force I have often, in a few seconds, retarded their motion many pulsations in a minute by strong pressure on one of the carotid arteries. An instance of this kind occurred in the case of the late Admiral X. His pulse was quick, and already very full and tense. Pressure on one carotid almost instantly reduced the pulse fifteen or twenty beats in a minute, without having previously increased either its frequency or strength ; the pulse returned to its former state as soon as the pressure was removed."

The carotid artery contains the receptor part of the mechanism, the glossopharyngeal nerve conveys the impulse to the medulla ; here the impulses exert two chief influences—they inhibit the heart and they depress vasomotor tone. This remarkable and seemingly purposive grouping of reflex cardiovascular effects also occurs when the depressor nerve is stimulated (see Kisch,[7] and Heymans and Bouckaert[8]) ; it must surely depend, therefore, upon a close linkage of the efferent channels by central parts of the nervous mechanism. And, given this linkage, is it not highly probable that the central and efferent parts of this same mechanism are disturbed in the clinical syndrome of vasovagal syncope, in which strong vagal effects are likewise combined with depressor vasomotor effects?

* In our previous account the part played by the vasomotor system in inducing this form of syncope was insufficiently appreciated. The statement therein that the attacks may be relieved by atropine is inexact ; the slow rate is relieved, but, as the protocol (p. 26) illustrates, atropine does not promptly abolish pallor nor bring blood pressure back to normal.

The suggestion put forward is supported from another source. Pressure on the carotid in man gives rise to gastro-intestinal manifestations. According to Waller, a feeling of uneasiness and nausea develops, and increased movements of the alimentary tract are signalled by borborygmi. Danielopolu[9] recorded the movements of the stomach in man, and found these at first inhibited, and later increased in activity. The associated alimentary symptoms strongly suggest similar occurrences in vasovagal syncope. From the same point of view it would be interesting to know if sweating occurs as part of the carotid sinus reflex.

The evidence derived from respiratory changes is not so clearly in support. Parry first stated, in 1799, that pressure on the carotid in man causes respiratory distress, or as Waller and Czermak found, longer and deeper respirations (see also Recht[10]). Danielopolu and his collaborators[11] speak of increased rate and depth in man and dogs from the same procedure. But these changes are not quite relevant. The physical stimulus of a rise of pressure (within the carotid), while decreasing heart rate and blood pressure, also decreases the rate and depth of respiration, and ultimately leads to apnoea (Heymans and Bouckaert[12]). If vasovagal syncope is due to a disturbance of the same central mechanism, respiration should become slow and shallow ; but increased depth appears to be the rule, though it is not invariable. It is perhaps premature as yet to argue from such observations as have been made ; and it is to be remarked that the effect of diminished blood flow to the brain is known to increase respiration, and this effect may prevail in the clinical seizure.

If the suggestion proves fruitful, and the vasovagal seizures described are indeed set up through the same central and efferent mechanism, which takes part in the carotid sinus reflex, then, on clinical grounds, it would be legitimate to suggest that this mechanism can be set in motion through many afferent channels other than those at present recognized by physiology.

GOWERS'S SYNDROME

In the foregoing account, attacks have been described under the term "vasovagal." There is but one objection to the use of this term ; it is that is has been employed before by Gowers[13 14] to denote another condition. But the term is so entirely apposite to the form of syncope here discussed, and our knowledge of the other condition to which it has previously been applied is so vague, that the earlier usage, which has never become general, can be abandoned with advantage.

Actually, there is little real resemblance between the attacks that have been described and those of which Gowers wrote. His patients were usually women, epilepsy or insanity was sometimes found in the family history, minor epilepsy or migraine was frequently associated. The symptomatology varied and the picture he gave was not very definite. The attack usually lasted half an hour or more ; it would often bring inability to fix attention, *but no impairment of consciousness* ; sensations occurred in the epigastrium, but seldom nausea and never vomiting.

A sense of coldness in the limbs was frequent, and sometimes an accompanying tingling or a sense of ascending numbness of the limbs definitely stamped the case as migrainous. Shortness of breath (sometimes intense), precordial discomfort in the form of pain or palpitation, and a sense of dread, were among the symptoms. As Gowers says, the symptoms were mainly sensory and subjective. The pulse was said to become small, in one case almost imperceptible, the face to show pallor, though the latter, judging from the case reports, was inconstant, rarely conspicuous, and sometimes replaced by flushing.

Rigors developed in several cases, cramp-like spasm in others.

This is obviously a totally different condition from our syncopal attacks, and therefore dependent upon a distinct mechanism ; Gowers, unlike some later writers on the same subject, clearly recognized the distinction between his cases and those which he terms "simple cardiac faints." It is, indeed, most important they should not be confused ; while it is to be stated, in justice to Gowers, that he used the word "vagal," as he says, "as a descriptive term, without implying causation," the fact remains that such physiological terms cannot be employed without the corresponding inferences being drawn. So it is necessary to state that there is nothing in his description of what he terms "vagal or vasovagal" attacks that justifies the adjective "vagal" ; the evidence actually brought forward consists purely of the subjective feelings of the patient. The pulse rate was noted in one case only, and was in this increased. There is not much in his account to justify the idea of any profound vasomotor disturbance. Actually Gowers thought that the vasomotor centre was disturbed, causing constriction of the vessels, but facial pallor, and coldness of the extremities —if indeed this was usually objective—might result from splanchnic vaso-dilatation, just as readily as from vaso-constriction in the parts displaying it. However relevant Gowers's description may be to studies of nervous disorders, it has not helped us to understand cardiovascular syncope or vasomotor disorders, and the continued use of the term "vasovagal" to indicate these cases drawn from the borderland of epilepsy is, in the light of recent work, to be deprecated.

NOTHNAGEL'S SYNDROME

The clinical description given by Gowers was thought by him to resemble an earlier picture painted by Nothnagel,[15] under a term that has likewise caused confusion—namely, "angina pectoris vasomotoria." Their identity appears to have been accepted by more than one writer (Ryle,[16] and Collier[17]) on evidence that is suggestive but cannot be regarded as conclusive. I venture to think that further discussion of the matter on the basis of the original reports can hardly fail to prove sterile, since these are scarcely adequate for the final identification of either malady ; and that what we require is a closer examination and description of patients of the kind while in the attacks. So far as the cardiovascular system is concerned, Nothnagel's description is more precise than that of Gowers. Nothnagel's four patients had no heart disease ; three of them were men in their thirties and forties. The attacks were provoked by cold or by bouts of drunkenness. The common signs in the attacks were blanching of the skin, the hands or limbs being involved conspicuously and displaying numbness and coldness ; the pulse was narrow and small, its rate was unchanged or dropped. These signs preceded anxiety or actual fear, palpitation, and giddiness. The attacks lasted a quarter of an hour to one hour ; consciousness was not lost. In one of his cases, the only elderly subject, anginal pain appeared. Nothnagel's syndrome is seemingly a rare malady, for no clear records of it appear to have been added since he wrote, unless we include the cases of Powell[18] and of Stokes,[19] in both of which, however, the pulse rate rose (Lewis[20]). Stokes's case is notable because it is the only one of the series in which actual blood pressure readings were taken ; these were raised.

Nothnagel's evidence of vaso-constriction was chiefly the occurrence of conspicuous pallor and coldness of the extremities. Pallor of the skin, with or without coldness, is, in fact, inconclusive evidence of vaso-constriction ; pallor is a sign of diminished vessels ; oncoming coldness, when objective, is a sign of diminished blood flow. Both these signs can appear when the main vasomotor change is one of vaso-dilatation in other areas ; especially is this true of the facial skin, which drains easily, though the limbs may be affected similarly to a certain point. The onset of facial pallor is obviously quite inconclusive evidence of vaso-constriction. The quick onset of conspicuous pallor of hands and feet, providing these are not held aloft, is a more certain sign of vaso-constriction. Nothnagel stressed the signs of vaso-constriction as the first event, appearing several minutes before the major symptoms. He states this to have been the order of events in three of his four cases. His was a slender series, but the important idea which it suggested—namely, that vaso-constriction, by throwing a considerable burden on the undiseased, though not necessarily wholly efficient, heart, can determine secondary symptoms of considerable or severe distress—receives support from a different source. Severe palpitation, great anxiety and apprehension, throbbing in the neck, a sense of oppression in the chest, pain in the chest of anginal type, are all symptoms that may be provoked in healthy subjects by the action of adrenaline in man, the symptoms being associated with raised blood pressure and acceleration of the heart. In paroxysmal hypertension, thought to be due to adrenaline released, a closely corresponding group of symptoms and signs develops, though intense headache, nausea, and vomiting may be added.

If we say that Nothnagel's syndrome is consistent with general vaso-constriction, and that this would explain the symptoms displayed by his patients, we probably state quite as much as is justified. It seems unreasonable that we should continue to base discussions of vaso-constriction upon what is largely guesswork, while the essential facts are there for the collecting ; or that we should continue to be saddled by terms which, by implying more than has been proved, tend to confuse our thoughts. It is difficult to see how a fresh publication of case notes that fail to add to knowledge can make for progress ; what is wanted is close study of patients in attacks with a clear identification of pressure and pulse changes and concomitant symptoms. It seems almost too self-evident to state that our understanding of transient derangements of the circulation must depend upon our directly ascertaining whether the blood pressure rises or falls and what happens to the pulse rate. Yet these, more often than not, are just the data that are not available, and so knowledge of vasomotor seizures in man remains more obscure than it should remain.

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