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VISCERO-CUTANEOUS ANÆMIC ZONES AND THEIR SIGNIFICANCE.*

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It is an old experience that visceral diseases (e.g., digestive disturbances) are frequently accompanied by cutaneous hyperæsthesia. As early as the beginning of the nineteenth century the condition was described by Brodie, and later by Tod and Briquet, who interpreted it as local hysteria. In 1856 the Danish investigator, Fenger, advanced another explanation. In his studies on cardialgia he had excellent opportunity for observing this hyperæsthesia, which he believed was due to sympathetic disease of the intercostal nerves. This view held its ground until C. Lange, in his work on the pathology of the spinal cord, and in an article in the *Hospitalstidende*, 1875, proposed the theory that the hyperæsthesia must be interpreted as reflex pain. During abdominal operations, without narcosis, it was found that the abdominal organs were practically insensitive. They could be cut, torn or hacked about without the patient's feeling any pain. On the other hand, it was certain that under other circumstances very acute pain might be felt in the same organs. Lange explained this fact on the ground that the irritation from the diseased but insensitive organs was conducted by afferent sympathetic channels to the spinal cord, where it spread over the

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cerebrospinal tracts, afterwards being projected by the brain to the ends of the spinal channels in question.

Lange's theory attracted but little notice for some years, but in 1888 Ross published in *Brain* an article on reflex pain, which embodied views of a similar nature to those which Lange had championed. Some years later Head took up the subject * and discovered that the cutaneous hyperæsthesia corresponded to zones in which herpes zoster was localised—the so-called zones of Head.

Independently of Head, K. Faber carried out a series of investigations at Frederik's Hospital on patients suffering from digestive diseases.† Faber's results did not agree with Head's. The hyperæsthesia did not always follow Head's zones, but both investigators interpreted it as a reflex phenomenon in accordance with Lange's theory. A similar conception was held by Mackenzie. As early as the '90's he had begun his studies, which to a great extent formed part of his daily practice. His interpretation was similar to that of the above-named investigators. A stimulus proceeds from the irritated organs through afferent sympathetic channels and develops in the spinal cord an irritable focus, from which the stimulus spreads to centres in close proximity. In this way arise an efferent visceral reflex, a visceromotor and a viscerosensory reflex. The visceromotor reflex arises by muscular contraction of definite areas of the abdominal wall. The viscerosensory reflex is accompanied by a cutaneous, subcutaneous, muscular, or subserous hyperalgesia.

Mackenzie has utilized these reflex investigations for determining the seat of visceral diseases, and in his work on *Symptoms and their Interpretation*,‡ he has given a comprehensive account of his experiences and observations. His investigations comprise cases of disease of the heart, gastro-intestinal canal, genito-urinary organs, peritoneum, and pleura, and he shows by a series of examples what benefit may be obtained, both in private practice and in hospital, by a detailed knowledge of the visceromotor and viscerosensory reflexes, since with the help of them alone we can often trace the diseased organ. His investigations attracted considerable notice, not only in England, but also in Denmark, and, at any rate, among the younger generation of doctors, a good deal of interest was aroused in this subject in the latter country, so that a zealous search was made for visceral reflexes as soon as a case of visceral disease was encountered which was difficult to diagnose by the usual methods. Interest soon seemed to fade away, however, the reason being that the method often failed in those cases where it was most needed, namely, in incipient cases. In these no muscle rigidity

* *Brain*, 1893, 1894, 1896.

† *Hospitalstidende*, 1899.

‡ *Symptoms and their Interpretation* (London, 1912).

is found as a rule, so that we cannot avail ourselves of the visceromotor reflexes.

There still remains the investigation of the reflex hyperalgesia, but even this, when carried out in the orthodox manner with a needle or by pinching the skin, may be associated with great difficulty. We have only the patient's statement to rely on, and usually in such cases of mild cutaneous hyperalgesia he is unable, with even tolerable accuracy, to define the limits of the hyperalgesia. It is, therefore, often practically impossible to map it out correctly in this way, and if one is uncertain of its situation one naturally cannot draw conclusions about the seat of the disease.

Personally, I have employed these methods of investigation since 1914, but they have often failed because the patient's statements were far too vague and uncertain to base a diagnosis on, and I know that many of my colleagues have had similar experiences.

By a different method of investigation I consider that I have found that Head, Faber, and Mackenzie arrived at inaccurate or even quite erroneous results, and if the experts themselves can make mistakes, it is naturally still easier for the less practised and experienced observer. The method of investigation I refer to was briefly described in the *Ugeskrift for Læger*, November, 1920, under the title "Æsthesioscopy." The method consists in exposing the patient and allowing the surrounding air to cool the area of skin to be examined. The effect of the cold is reflexly to produce a mild ischæmia of the skin, which is most pronounced in the hyperalgesic area. If the skin is now examined in subdued light a white portion is observed in contrast to the surrounding skin, and if it is approached from all sides with a small fine needle it will be found that its limits accurately correspond to those of the hyperalgesia.*

Simple as the method perhaps appears to be, it is the outcome of a series of preliminary orientating experiments.

On investigating the sensations of heat and cold it became evident that the hyperæsthesia, besides being a hyperalgesia, was also a thermo-hyperæsthesia, that is to say, not only were the nerves for the perception of pain hypersensitive, but also those for the perception of heat and cold. Now it is generally acknowledged that many, particularly old persons, are susceptible to cold; in other words, they are usually sensitive

* In cases where the skin is previously anæsthetic we see (provided that the anæsthesia is not of central origin) the reflex anæmia make its appearance with undiminished strength, but in such cases, of course, we are unable to make control tests with the aid of a needle.

If the anæsthesia is due to partial destruction of the cutaneous nerves, the remaining ones may cause cutaneous anæmia. The area may be hypæsthetic instead of hyperæsthetic to the needle. The above cases are, however, only exceptions. The rule is that the anæmia covers an area of hyperæsthesia which can be mapped out with a needle.

to small changes of temperature, while they perhaps react relatively slightly to painful stimuli. It occurred to the author, therefore, to try the action of cold for mapping out the hyperalgesia with the aid of the patient's statements as to where the cold feeling was most marked. As a cold stimulus a light ether douche was used, which by its rapid evaporation on the skin provoked a pronounced feeling of cold. In some cases rather more certain information could be elicited by this means than by the pricking or pinching methods, but there was always the drawback that one had to be entirely guided by the patient's statements. It was clear that if the investigator could alienate himself from the patient's interpretations and statements, and himself obtain accurate information about the situation of the hyperalgesia, the method would gain in value as an objective mode of investigation in contrast to the ordinary subjective-sensation technique employed.

In view of the fact that the nerves for both heat and cold were hyperæsthetic, we should have expected that by means of equal hot and cold stimuli we could produce a dilatation or contraction of the cutaneous vessels respectively—particularly marked in the hyperæsthetic area and visible against the surrounding skin. A trial with a hot stimulus, however, did not come up to expectations. It is true that with this stimulus easily perceptible, viscerocutaneous hyperæmic zones could be brought into relief. If, for example, an appendix hyperalgesia is treated with hot fomentations and these are quickly removed, an evanescent redness is frequently observed, localized in the same zone, which can be mapped out by mechanical irritation or by that produced by cold. After prolonged application of fomentations we may also see a rather persistent hyperæmia, which may easily be detected, even by the inexperienced investigator, but the form is more diffuse and less sharply circumscribed. In addition to this, it is of a fleeting nature, in contrast to the cutaneous ischæmia which quickly supersedes it when the patient is undressed. Finally, to elicit it an apparatus is required, which, although simple, is more complicated than in the case of the cutaneous ischæmia, which becomes established as soon as the patient is exposed to the mild action of the cold exerted by the air at ordinary room temperature.

It necessitates some practice to detect this poorly pronounced anæmia, but the same applies to most of the other clinical methods of investigation, and if care is taken to examine in diffused light, excluding direct light and intermingled reflections, the investigation is not difficult; moreover, it is simple and not dangerous.*

* The anæmia is most readily observed by daylight. But also at night the examination can be made without difficulty, most easily by using green light. The investigator places himself in front of the source of light in such a way that his

With the aid of this method I have examined about 3,000 patients since the spring of 1920. The majority of these came from private practice and the provincial hospitals. Since the spring of 1921 I have had the opportunity of examining about 800 patients in this and other departments of Frederiksberg Hospital. The above figures are only approximate. I did not keep an accurate record, nor would it have been of much interest, as most of the cases were simple and straightforward cases of visceral diseases, like tracheitis, bronchitis, pneumonia, gastritis, enteritis and colitis, and as regards the genito-urinary system, cystitis and pyelitis, births and abortions.

The method has, of course, no diagnostic importance in these easily recognisable diseases, but the reason that the number of cases investigated is relatively so large is that I have consistently examined every patient whom I have had the chance of investigating, both in hospital and private practice, for cutaneous anæmia. I have thus been able to get an impression of the distribution of reflex hyperalgesia in different visceral diseases, which, even if at times it needed deeper study, nevertheless allows one to deduce some general rules regarding the occurrence of reflex hyperalgesia.

The best-marked cutaneous anæmia is seen in those cases where there is an attempt to overcome the obstruction of some canal by tonic contraction of smooth muscle, e.g., in cases of intestinal obstruction and colic of different kinds. As the pain increases in strength the anæmia gradually becomes greater, but always in a proximal direction, while the distal limits are unaltered. The lower boundary, however, is sharper and more clearly marked off from the adjacent skin, while the upper boundary is more diffuse and vanishes in the proximal direction. This extension of the hyperalgesia in the proximal direction was previously described by Mackenzie, and his explanation of it, which is undoubtedly the right one, is that the distal boundary corresponds to the site of the stricture. The colic is initiated by the muscles immediately proximal to the obstruction endeavouring to overcome it by violent contraction. By degrees, as more and more muscles take part, the pain and irritation spread to higher segments, and in conjunction with this the anæmia increases. But on the distal side of the obstruction the spasm yields and, therefore, reflexes do not proceed from this

shadow is projected on the patient's skin. The anæmia then shows up as a light zone against the surrounding darker parts.

The examination by daylight is conducted on the shaded side by turning the part of the skin to be investigated away from the light, or a screen (perhaps the investigator himself) is interposed between the patient and the window so that the shadow is projected on the patient's skin. Furthermore, the investigator must wait a minute or more until his eye gets used to the light, and until the vaso-constrictor reflex is put into action. The anæmic zones are then observed, as a rule, without difficulty.

The examination can also be made on jaundiced skin but it is rendered difficult if the skin is previously anæmic, or very hairy.

part, nor does it cause reflex cutaneous anæmia. The distal boundary of the cutaneous anæmia thus corresponds to the site of the obstruction. If on the basis of this we wish to determine, for example, the afferent segmental innervation of the alimentary canal in the whole of its extent, we must have at our disposal many cases of stenosis of the canal or the ducts of the corresponding glands, preferably verified by operation. Such material has not been at my disposal, but a close estimate may be obtained from the cases I have observed.

Although cases of stenosis of the gastro-intestinal canal or the ducts of the glands belonging to it, which have been confirmed by operation or *x*-ray examination, are relatively poorly represented in my material, most of the cases of reflex anæmia I have observed have been caused by gastro-intestinal disturbances. In the summer of 1920 alone, during an epidemic of febrile painful gastro-enteritis, I had the opportunity of following the course of reflex anæmia in about sixty patients, from the beginning to the end of the illness. Later on these observations were supplemented by a large number of a similar kind in patients with mild and transient digestive disturbances, such as it is every busy doctor's lot to see in daily practice and in the hospitals. These cases, which otherwise do not greatly attract the attention of the investigator, have been of particular interest to me, since, with their constantly accompanying, double-sided and centrally situated reflex anæmia—apparently subject to some law—they have suggested to me the idea that is the central one in the whole method of investigation: *Double-sided reflex anæmia is present in diseases of unpaired organs, and one-sided anæmia in diseases of paired organs*, as will later be further emphasized. But it has not been of use in determining the level of the seat of the disease because, although we can assume that an acute and painful abdominal disease attended by diarrhœa with pathological stools is due to a lesion of the unpaired organ, the intestinal canal, there will always be doubt as to the segment in which the disease is mainly or exclusively located. With the experience I have acquired from my present cases I consider that, within certain limits, I can determine it with the help of æsthesioscopy alone. The various facts relating to the diagnosis of the level have been obtained from relatively few but, on the other hand, definite cases, where the diagnosis was either verified by operation, post-mortem examination, or *x*-ray investigation, constituting a total of fifty.

In the acute gastro-intestinal affections the reflex anæmia may gradually spread over the whole abdomen as the disease progresses. Such an extensive reflex anæmia is seen only extremely rarely. The rule is that the anæmia occurs in four phases. If one is called to the patient shortly after the pain has started, a reflex anæmia such as is shown in *Fig. a-d-f-e* is found. As will be seen later, this anæmia

does not correspond to that which is observed in isolated gastric diseases, but to that observed in gastro-duodenal affections, which is presumably accounted for by the fact that the infection usually does not give rise to clinical manifestations until the duodenum is involved in the morbid process. Afterwards the anæmia spreads, with its lower edges pointing obliquely downwards towards the umbilicus (*Fig. a-d-g-e*). The next

(For meaning of figures see under last illustration.)

phase is a periumbilical anæmia (*Fig. 3*), often with somewhat curved borders, but most frequently bounded by straight lines. This kind is most often associated with acute diarrhœa. It corresponds to irritation of the small intestine, and is usually well defined and easy to observe. The third phase is the infra-umbilical anæmia of colon affections which, when the sigmoid is included, extends to the symphysis and then appears on the back as a similar symmetrical anæmia situated

in the lumbar segment region. The fourth phase is the rectal anæmia, occurring exclusively on the back (see *Fig. 16*).

These facts could be adduced with a good deal of certainty from the diagnostic reasoning, commonly employed long before definite criteria could be obtained from cases of stenosis. But such observations could not form the basis for any certain estimation of the level of the lesion. For this purpose, as already explained, a number of accurately diagnosed stenosis cases are required. With the aid of those which constitute my material, however, I maintain that I am able to a great extent to establish the segmental demarcation of reflex anæmia for the various segments of the intestinal canal, and at the same time, also, their afferent sympathetic innervation. This must correspond to the segmental situation of the cutaneous anæmia. If this were not the case the visceral reflexes would be abolished by transverse lesions of the cord, which does not happen. As will be later explained, experimental investigations are in favour of the view that reflex arcs are unisegmental, so that it is permissible in definite cases to determine the afferent sympathetic innervation of the segment of an organ from the segmental position of the lower boundary of the corresponding anæmia.

Four cases of stricture of the cardiac end of the stomach, one of which was confirmed by *x*-ray examination and one by post-mortem examination, were accompanied by cutaneous anæmia, as shown in *Fig. 1*, with the lower border running through the 5th and 6th dorsal segments. Three cases of pyloric stenosis (seen by *x*-rays) showed reflex anæmia corresponding to *Fig. a-b-c*—therefore with the lower border at the boundary between the 8th and 9th dorsal segments. The afferent channels of the stomach must therefore go principally to the 6th, 7th and 8th dorsal segments. Eight cases of cholelithiasis were associated with reflex anæmia, with the lower border running horizontally through the 9th dorsal segment. The opening of the common bile duct must then correspond to the 9th dorsal segment, and the part of the duodenum above it to the 8th and 9th dorsal segments.

An unmarried man of twenty-seven who, with a suicidal purpose, had drunk about 100 c.c. concentrated corrosive sublimate solution, was admitted to hospital an hour after swallowing the poison, and the stomach was washed out with 12 litres of water. A quantity of blood-clot was found in the washings, indicating a considerable erosion of the mucous membrane. The reflex anæmia at this time corresponded to *Fig. a-b-c*, and therefore the case was looked upon as an isolated diffuse affection of the stomach. In the next few days the anæmia spread in a distal direction, the lowest point reaching to about the boundary between the 9th and 10th dorsal segments, and the duodenum must, therefore, now have been attacked by the irritative process.

In association with this the anæmia localised in the spinal region of the

back was observed to spread in a distal direction, but was quickly arrested. The small intestine or, at all events, the large intestine, could therefore not be directly implicated in the lesion.

Five cases of duodenal ulcer were accompanied by anæmia, as shown in *Fig. a-d-e-f*, from which we can conclude that the duodenum's afferent innervation must, at least, reach as far as the middle of the 9th

(For meaning of figures see under last illustration.)

dorsal segment. It probably extends as far as the 10th dorsal segment, judging from the following case.

A woman of seventy-eight had an excision of the pyloric region performed for ulcer of the pylorus, and afterwards closing of the gastric ulcer and duodenal ulcer, as well as a gastro-enterostomy, after measuring off 50 cm. of small intestine. About a fortnight after discharge from hospital she sought readmission for an attack of intestinal obstruction (bile-stained vomiting, constipation, absence of flatus, pain and tenderness in the epigastrium, fever,

and small, soft pulse). By means of æsthesioscopy a reflex anæmia resembling one of duodenal origin was found, which extended to the 10th dorsal segment in the middle line. Judging from this the pain ought also to have been emanating from a duodenal lesion. The vomit was bile-stained, and thus the passage from the common bile duct through the anastomosis to the stomach must have been free. At first we might therefore assume that the obstruction was due to the closing of the distal loop of the anastomosis; its position was known precisely. Providing the diagnosis was correct, this would afford the opportunity of determining the segmental position of the piece of small intestine in question.

At the operation, however, an abscess was found originating in the duodenal blind sac, and perforating it by successive periduodenal layers of pus. The case is useful as illustrating the reliability of the method, but for accurate determination of the segment it could not be employed.

As mentioned above, duodenal reflex anæmia extends, at any rate, to the lower boundary of the 9th dorsal segment. This being so, the small intestine must practically belong to the 10th and upper part of the 11th dorsal segments. It is, perhaps, rather surprising that in view of the length of the small intestine, it corresponds to so few segments. It must be so, nevertheless, for, as stated above, the duodenal anæmia reaches, at least, to the lower border of the 9th segment, and the ilco-cæcal portion belongs to the upper half of the 11th dorsal segment. This is based not only on the fact that a case of ilco-cæcal obstruction was accompanied by anæmia, the lower border of which just reached the point named, but also because appendicitis is sometimes associated with narrow periumbilical areas of anæmia (in which case we may expect to find an isolated appendix) and sometimes by infra-umbilical areas of anæmia, when we may expect to see perityphlitic adhesions at the operation, or principally changes which indicate an accompanying lesion of the colon.

The remainder of the intestinal canal corresponds to the sacral and lumbar, as well as the 12th and partly the 11th dorsal segments. The ascending, transverse, and descending colon reaches to the lower boundary of the 12th dorsal segment, while the sigmoid flexure of the colon and the rectum belong to the lumbar and sacral segments. The boundary between the last two seems to correspond to the 3rd lumbar segment; at any rate, the following case was diagnosed on the basis of this assumption.

An unmarried sailor of forty was treated for subchronic enteritis on account of continuous diarrhœa. Nothing abnormal was found on rectal examination, nor on palpation of the abdomen. But by means of æsthesioscopy lumbar anæmia was discovered on the back with the lower boundary running through the 3rd lumbar segment, and, in front, a narrow anæmic band in the lower part of the 12th dorsal segment. The disease could not be

due to a rectal lesion because, as is seen in cases of carcinoma of the rectum, it would then be associated with anæmia extending to the sacral segments, perhaps as far as the 5th.

Presumably, therefore, the disease depended upon a deep-seated affection

Reflex anæmia observed in : (1) Stricture of the cardiac end of the stomach.—(a-b-c) Pyloric stenosis.—(a-d-e) Cholelithiasis.—(a-d-g-e) Duodenal ulcer.—(3) Enteritis.—(4) Colitis.—(5) Tracheitis.—(6) Bronchitis.—(7) Asthma (br).—(8) Uterine disease.—(9) Pneumonia.—(10) Pericarditis.—(11) Angina pectoris.—(12) Aortitis.—(13) Gastritis.—(14) Enteritis.—(15) Colitis.—(16) Carcinoma of the rectum.—(17) Aneurysm of the aortic arch.—(18) Bronchitis.—(19) Renal calculus.—(20 and 21) Hyperæsthesia in traumata.—(22) Ureteric colic.

of the colon or a lesion of the sigmoid. At the operation a constricting inoperable carcinoma of the sigmoid was found.

To the most frequent and most easily diagnosed æsthesioscopic findings belongs infra-umbilical colitis anæmia. We had a particularly good case in the hospital.

A male paralytic of thirty-seven complained one day of violent pain in the abdomen, which was accompanied by thin stools containing a good deal

of blood. The blood was bright-coloured and liquid, so that the possibility of a foreign body having been introduced into the rectum was considered. The patient was resentful and violent—several of the *personnel* had damaged faces in witness of his spitefulness. Exploration of the rectum would therefore be difficult, and probably further provoke the patient.

It was, therefore, an advantage to be able to dispense with this examination and make a diagnosis of the level of the lesion. As often as the patient was covered up he tore the clothes off himself, and frequently lay naked in his bed. A well-defined infra-umbilical anæmia then appeared on the abdomen, as depicted in *Fig. 4*. The pain must, therefore, have been due to a colon infection, and the cause was not far to seek; on account of a strong Wassermann reaction he had received a test injection of calomel the day before in double the usual dose (0.10 grm.).

To the most definite and unmistakable viscerocutaneous anæmias belong those which can be observed during the pains of labour and which disappear in the pauses. There is no doubt in this case that the factor causing the pain is the uterine contraction.

Uterine reflex anæmia is usually first seen and most marked on the back, where it occupies the same segments as rectal reflex anæmia (*Fig. 16*), a fact which explains why it is that a woman in labour is occasionally surprised by the birth of her child during a visit to the lavatory, because she has confused the early labour pains with tenesmus. But in addition, we usually see epigastric anæmia (*Fig. 8*), and finally, the stimulus may spread to the lowest dorsal segments, when an ascending cutaneous anæmia may be observed in front, which during strong pains may reach right up to the epigastric anæmia.

As in the case of gastro-intestinal disease, this kind of anæmia is also represented in the spinal region. In this and subsequent cases the most marked anæmias will be principally dealt with—those which are applicable for diagnostic purposes.

As already mentioned, we usually also find in uterine diseases a rather extensive, although less distinct, epigastric anæmia (*Fig. 8*). The reason that uterine diseases are accompanied by reflex anæmia at such widely different levels, I think, must be sought for in the fact that the arterial supply of the uterus comes partly from the uterine artery and partly from the internal spermatic artery. Everywhere in the body we find an intimate association between the vessels and the surrounding tissues, which might indicate that the afferent channels of the vessels as well as the surrounding tissues go to the *same* spinal segments, and are then directly connected with reflex arcs; otherwise transverse lesions of the spinal cord would be attended by marked vasomotor disturbances, which is known not to be the case, any more than that the cutaneous visceral reflexes are put an end to in such cases.

If we proceed on the assumption that the above explanation is correct, it is intelligible that the uterine tissue supplied by the internal spermatic artery may cause, when stimulated, the cutaneous anæmia at the high level, while that supplied by the uterine artery will occasion the anæmia at the lower level.

Appendicitis and colitis also often occasion a similar epigastric anæmia without being supplied by arteries of high origin. The cause in this case is to be found in the disposition of the omentum. This structure starts from the stomach, is firmly attached to the colon, and in appendicitis it is frequently adherent to the appendix. In such cases every movement of the patient induces slight pain by dragging on the omentum. It is supplied, however, by the cœliac artery, and thus its afferent sympathetic channels must go to the high-level segments, which is in harmony with the fact that the pain is felt in the stomach and that the reflex hyperalgesia is situated in the epigastrium.

Experimentally, analogous conditions can be shown to exist in cold-blooded animals. Fish (eel or cod) are principally used as experimental animals, and they are decapitated to ensure the presence of spinal reflexes only. If a piece of the intestine of an eel is stimulated by a faradic current, a marked intestinal spasm is momentarily produced. If the gut is stroked up and down a few times with two needle-shaped electrodes 2 mm. apart, a tetanic contraction is evoked, which may continue for several hours.

If now we investigate the reflex irritability of the skin by passing electrodes (between which there is a weak constant or faradic current flowing) slowly along it, we shall observe that the part outside the skin area corresponding to the stimulated portion of gut reacts more briskly than the rest of the skin. This is an experimental viscerocutaneous hyperæsthesia which, on account of the animal's segmental constitution and intestinal canal of rather straight course, is located in the skin at the level of the stimulated portion. If the experiment is repeated after about fifteen minutes' interval, it is found that the irritability, instead of being increased, is now depressed in comparison with that of the rest of the skin; and if it is repeated again twenty minutes later, practically no muscular contraction is produced by stimulating the part in question.

The reason of this is easy to demonstrate. If the eel is lifted up it is found that the part we are dealing with is as rigid as a stick, while the parts above and below are relaxed. The muscles of this part of the body are in a state of tetanic contraction, and so no further muscular contraction can take place, that is to say, we have an experimental visceromotor reflex. These phenomena are equally well marked on both sides.

Experimentally we can also produce viscerocutaneous reflex anæmia by means of adrenalin injections. If, for example, we inject

into the spleen of a decapitated eel, whose circulation is stopped by preliminary ligature of the heart, about 0.1 c.c. of a 10 per cent. adrenalin solution, we shall observe, after a few minutes' interval, white patches appearing on the skin at the level of the spleen, and always bilaterally.* In a successful experiment the skin becomes as white as snow, but it is always distinctly anæmic. Good bilateral cutaneous reflex anæmia is also seen on injecting adrenalin into the gall-bladder, and on painting the surface of the intestine and liver with it. Sometimes the anæmia assumes exactly the same form as is always observed in man, i.e., fan-shaped, with the base towards the middle line, but as a rule we only get anæmia of more irregular form, and it must be added that genuine and well-marked reflex anæmia is often accompanied by a less distinct general anæmia, which must be due to a reflex through a higher vasomotor centre. Experimental cutaneous anæmia is not quite comparable with that observed in patients, but it should be remarked, at any rate, that injection in unpaired organs (spleen, gall-bladder, etc.) is always accompanied by double-sided cutaneous reflex anæmia.

That the vessel reflexes involved are of spinal origin is proved by the fact that all the animals were decapitated; but we may further conclude that the reflex must be unisegmental, since it is not abolished, although the spinal column is carefully divided from behind. On both sides of the section which pass through skin, muscles, and cord, the cutaneous anæmia extends to the dorsal middle line. The reflex must, therefore, occur in the various intact segments. In agreement with this we must assume that experimental viscerosensory and visceromotor reflexes take place by means of unisegmental reflex action.

But the main point is, that the cutaneous and muscular reflex phenomena of spinal origin, which can be elicited by stimulation of the muscles of the viscera, are located in the same region of the body as the first and most marked cutaneous vaso-constrictor reflexes to appear through the local action of adrenalin. It must be concluded from this that the muscular afferent sympathetic channels of the viscera and the corresponding afferent channels of the vessels have the same segmental innervation; in other words, from a knowledge of the arterial supply of an organ innervated by the sympathetic system, we can predict what the afferent nerves of the organ will be, and consequently the site of the cutaneous visceral reflex phenomena. Similar conditions must presumably apply to man, as has been shown in the case of uterine diseases and the organs furnished with omentum.

The visceral aortic branches have undergone changes during development, resulting in displacements and fusions, which make it

* The blanching is due partly to cutaneous anæmia and partly to cutaneous pigment retraction.

impossible to decide the segment an artery belongs to, directly from its place of origin. But the theory readily explains why cardialgia can so frequently accompany different visceral diseases, and conversely, from undoubted cutaneous reflex anæmia, the place of origin of which is known, we can predict the innervation of the organ's vessels and the segments to which they belong. When, for instance, one knows that gastric reflex anæmia is located in the 6th to 8th dorsal segments, one can conclude that the celiac artery corresponds to the 6th to 8th thoracic segments, irrespective of the fact that its origin is displaced in a distal direction, so that anatomically it belongs to the abdominal aorta. From considerations of space, a review only of the results which can be obtained from the theory will be given at the end of the article.

Reverting now to the æsthesioscopic observations in man, it is intelligible why we observe prostate diseases attended by reflex anæmia of the same distribution as that of uterine diseases, usually only visible on the back (*Fig. 16*). A prostate reflex anæmia was the first case I had the opportunity of examining. It was that of an unmarried man of nineteen, who had pyuria and lumbar pain, and was admitted for treatment for pyelitis. In a dim light distinct anæmia of the skin could be seen corresponding to the seat of the pain. The situation was as shown in *Fig. 16*, and therefore pyelitis could not be the cause. On exploring the rectum a tender and enlarged prostate was found, and a microscopic examination of the urethral secretion disclosed the gonococcus.

Diseases of the Fallopian tubes and ovaries are but seldom associated with well-marked anæmia. It is situated in the 10th to 12th dorsal segments, with possibly secondary cutaneous anæmia in the 7th to 9th dorsal segments.

In the case of the kidneys I have often seen reflex cutaneous anæmia accompany pyelitis. It is more pronounced in the case of renal calculus, being practically always unilateral (*Fig. 19*). Gradually, as the stone slips further down the ureter, the lower border of the anæmia, which is now more distinct in front, is displaced further and further down towards the symphysis (*Fig. 22*).

I have no data referring to pancreatic and splenic diseases. Judging from the place of origin of the arteries supplying these organs, the position must roughly agree with the anæmic zone of the stomach and biliary passages. Diseases of the heart and pericardium are also frequently attended by reflex anæmia. As a rule it is not so marked as that we see in gastro-intestinal diseases, but distinct enough to be discerned. The reflex anæmia is bilateral, as elsewhere, when it is a question of the unpaired organs. The position corresponds usually to *Fig. 11*, but I have also observed it corresponding to *Figs. 10* and *12*.

I have not had the opportunity of making a careful investigation of its lowest limits in stenosis of the different orifices. Presumably, diseases of the heart, coronary arteries, and the part of the descending aorta belonging to the 5th to 7th dorsal segments are represented by the same reflex anæmia, while diseases of the aortic arch produce anæmia situated at a higher level. Dr. Levison, the physician to the department, has reported to me a case of aneurysm of the aortic arch accompanied by well-marked, centrally placed bilateral and symmetrical cutaneous anæmia extending to the 6th cervical segment (see *Fig. 17*).

Lower level aortic segments must cause lower level reflex anæmia. Experience is lacking, however, in this connection, but we had the chance of observing in hospital a case of aortic thrombosis.

An unmarried woman of thirty-three, suffering from manic-depressive psychosis, complained one day of violent pain in the loin and in the front and sides of both legs. In the course of a few hours the patient became completely paralytic in both legs, which were anæmic, cold, and pulseless.

The bilateral condition in conjunction with the complete anæmia and cessation of femoral pulsation pointed to an aortic stenosis, which must have been situated just over the bifurcation, as the lesion was not accompanied by intestinal trouble. This would be the case if the mesenteric artery was involved in the process. At the autopsy a thrombus was found, as expected, which occluded the lumen as far as about 3 cm. above the bifurcation and extended downwards into both iliac arteries.

The extreme anæmia of the legs in this case naturally could not be looked upon as a visceral vaso-constrictor reflex, as it was merely the consequence of the lack of blood supply. But the pain radiated into the lumbar segments and missed the sacral segments, which is just the distribution we should expect to find in reflex hyperalgesia caused by aortic stenosis in the lower lumbar segments. On the back there was well-marked bilateral, symmetrical anæmia, corresponding roughly with *Fig. 15*.

In Mackenzie's work there is no mention of the reflex hyperalgesia associated with diseases of the respiratory organs. The pain which accompanies violent coughing is assumed by Mackenzie to be due to myalgia brought on by the excessive use of the respiratory muscles. During the influenza epidemics, however, I frequently saw such cases attended by cutaneous anæmia similar to that observed in other visceral diseases, which would seem to show that the pain is of reflex origin. This has been assumed by several other investigators, and a closer examination confirms this view. Tracheitis is associated with pain located in the region around the upper portion of the sternum, but pain is also felt well out to the side, that is to say, considerably outside the tracheal boundaries. In bronchitis, pain is felt further down on the front of the chest, or in the back, where we often find local myalgia ;

but in unilateral bronchitis the pain and the myalgia are also limited to one side. If the myalgia was caused by the excessive use of the respiratory muscles we should expect to find bilateral myalgia in unilateral bronchitis.

Asthma cases are often accompanied by what Rosenthal calls epigastric aura, that is to say, an oppressive sensation in the epigastrium, and in harmony with this there is an epigastric cutaneous anæmia (*Fig. 7*). That this pain must be of a reflex nature follows from the fact that its site is completely outside the pneumonic area. It is still more obvious that the pain which often ushers in pneumonia must be of reflex origin, since it is generally located in the hypogastrium and occasions attacks simulating appendicitis (*Fig. 9*). The anæmia is usually poorly developed and often difficult to see. Its position will be seen from *Figs. 5, 6, 7, and 9*.

The most important forms of visceral reflex anæmia that I have had the opportunity of seeing have now been briefly passed in review. In addition to these there are some which occur most frequently of all, of which we see numerous examples daily in the hospital, namely, those accompanying neurotic conditions, such as fear and depression. They disappear when the depression passes over into exaltation, and return when the depression takes possession of the patient again. In these cases we must presume that a triple reflex is involved :—

1. A psycho-visceral reflex, causing the visceral spasm.
2. A viscerosensory reflex, which leads to the cutaneous hyperæsthesia.
3. A spinal vasoconstrictor reflex, upon which the cutaneous anæmia depends.

We have, therefore, to deal with a psycho-visceral cutaneous reflex anæmia.

The application of the method in the diagnosis of peripheral neuritis and neuralgia of various kinds, as practised in the hospital, will not be further dealt with here. It need only be added that the action of the slight degree of cold afforded by the room temperature often does not suffice, in the presence of hyperalgesia of the extremities, to produce definite anæmia, for which reason we avail ourselves of a method devised by Levison and Haunö, where a cold air-douche is used which, even on the cool extremities, calls forth well-marked anæmia.

But it is necessary to point out that cutaneous anæmia may be observed to be a pure psychic vasoconstrictor reflex, for instance, frequently in traumatic cases and in persons who are operated upon, if their attention is directed in a morbid degree to the region of the operation. Irrespective of the fact that the operation may have been carried out satisfactorily in every respect, with perhaps perfect healing

and hardly any visible scar, we may observe poorly developed cutaneous anæmia of irregular form in these patients in the region in question. It is increased by the action of cold, but also by the amount of attention the patient bestows on it. From a diagnostic standpoint, there is no trouble in distinguishing this irregular anæmia, often of variable contour, from the visceral and psycho-visceral kinds which are always fan-shaped with the base towards the middle line, or from neuritic reflex anæmia, which corresponds to the distribution of the given nerve trunk.

Putting aside the last three forms of cutaneous anæmia, and comparing the results of the investigations into the viscerosensory reflex hyperæsthesia obtained by means of æsthesioscopy with those obtained by Head, Faber, and Mackenzie, it will be seen that there is want of agreement on several points. Reflex hyperæsthesia does *not* correspond to Head's zones, as Head found. Whether it is situated in front or behind, it has a fan-shaped form with the base towards the middle line, and even if the hyperæsthetic area encompasses several segments, the fan-shaped contour is maintained. Although it has been frequently stated above that the hyperæsthesia corresponds to one or more of Head's zones, this simply means that the distribution in the middle line corresponds to them, while out towards the sides it terminates in a pointed figure, as indicated in the accompanying illustrations.

The same thing has already been shown by Faber's investigations, where in some of the cases the reflex hyperæsthesia had precisely the same delta-like form as that observed by æsthesioscopy. On the whole, however, Faber finds that reflex hyperæsthesia corresponds roughly to Head's zones in position, on which point his results differ from those we obtain by observing the reflex hyperæsthesia outlined by the organism itself. But apart from this, twenty-four of Faber's thirty-four cases, at all events, must be incorrect, since they are recorded as unilateral hyperæsthesia. By æsthesioscopy we always see without exception reflex anæmia, originating in unpaired organs with sympathetic innervation, represented by double-sided, centrally placed symmetrical figures. In the case of the organs limited to one side of the body (for example, the appendix), the anæmia is found best marked on the same side, and in view of the fact that the hyperæsthesia is symmetrically placed, it can be understood that the patient's attention is exclusively fixed on the more pronounced hyperæsthesia, so that the milder anæmia on the opposite side is not noticed; for this reason the investigator's attention may be directed to the more marked hyperalgesia; yet the anæmia is always present on the opposite side also, and can usually be outlined with a needle.

The fact that reflex hyperæsthesia originating in unpaired organs

innervated by the sympathetic system is always bilateral must necessarily be fundamental, as it is the pivot on which the diagnostic conclusions obtained with the help of æsthesioscopy depend. We certainly cannot conclude that double-sided hyperæsthesia always emanates from an unpaired organ, seeing that it can originate in two simultaneously stimulated paired organs (for example, in cases of bilateral pyelitis). But we may conclude with certainty that unilateral hyperæsthesia originates in a paired organ, for in the case of an unpaired viscus it would, of course, have been bilateral. (With the help of æsthesioscopy we are thus able to distinguish unilateral epigastric renal reflex anæmia from that originating in the biliary passages, ureteric anæmia from appendix reflex anæmia, and so forth.)

As already remarked, the viscerosensory and visceromotor reflexes, as well as the viscerocutaneous reflex anæmia in the experimental investigations, originating in unpaired organs, were always bilateral. In view of the fact that Faber's investigations only dealt with reflex hyperæsthesia originating in the digestive canal, there can be no doubt that the results recorded as unilateral reflex hyperæsthesia must be fallacious. Head also found chiefly unilateral reflex hyperæsthesia, although relatively often bilateral in intestinal diseases. Nor was Mackenzie's attention directed to this point. Thus, in his work, reflex hyperalgesia in cholelithiasis and angina pectoris is described as unilateral. On the other hand, reflex hyperalgesia originating in the gastro-intestinal canal is depicted as centrally disposed but in rounded areas which depart considerably in shape from those observed by æsthesioscopy. The estimation of the level at which it occurs, however, agrees with what I found in my cases, as, in harmony with Mackenzie's finding, I observed, for example, that reflex hyperalgesia in the case of the gastro-intestinal canal is not dependent upon the situation but upon the distal position, so that reflex hyperalgesia from a part of the colon situated at a high level occupies a lower position than corresponding hyperalgesia arising from a loop of small intestine which has fallen down.

In accordance with this, we find that reflex hyperalgesia associated with the respiratory organs is arranged according to its remoteness from the centre.

Thus, the order is tracheal reflex hyperalgesia; below this, hyperalgesia originating in the bronchi; next, asthma hyperalgesia, which must arise in the bronchioles; and lowest, pneumonia hyperalgesia, which may reach to the lower border of the 12th dorsal zone of Head. E. Zak (*Wien. klin. Wochenschr.* 1919-20) has previously described hyperæmic, half-moon-shaped skin zones, which can sometimes be observed in visceral diseases (diseases of the aorta, for instance). The author interprets these hyperæmic zones as the result of viscerovasodi-

lator reflexes comparable with the previously mentioned viscero-motor reflexes. This explanation is undoubtedly erroneous. I have frequently had the opportunity of observing similar hyperæmic zones, but they are found on the border of the anæmic zone and are, undoubtedly, merely to be regarded as stasis phenomena caused by the blood from the anæmic area of skin being forced out into the anastomosing cutaneous vessels.

The following are the general rules relating to the occurrence of reflex hyperalgesia which can be deduced from the results of the investigation :—

1. Reflex hyperalgesia originating in *unpaired* organs is always *bilateral*.
2. *Unilateral* reflex hyperalgesia is due to diseases of *paired* organs.
3. The organs have the same afferent innervation as the vessels supplying them.
4. The lower border of the reflex hyperalgesia in cases of obstruction of a lumen corresponds to the afferent segmental innervation of that part of the organ which lies immediately proximal to the obstruction.

The detection of the organ involved must be made with the help of (1), (2), (3), and (4), and the diagnosis of the level of the disease with the help of (4).

If, for example, we are dealing with a case of appendicitis, we know from (1) that any accompanying reflex hyperalgesia will be bilateral, as the appendix is an unpaired organ. If we find marked unilateral hyperalgesia or hyperalgesia which only crosses the middle line by a narrow margin, we know that it must arise from a paired organ. First of all, one would think of the ureter or disease of the Fallopian tubes, and make an investigation in this direction. But the lungs are also paired organs, and pneumonia, as is known, may be ushered in by attacks resembling appendicitis at a time when the stethoscope yields negative results. In conjunction with rising temperature, pseudo-appendicitis pain might possibly be taken as an indication for operation. In such a case the æsthesioscopic picture would prevent the misconception. Personally, I have twice warned against operation on these grounds, and in both cases a right-sided croupous pneumonia eventually developed.

In a similar manner renal colic can in certain cases be distinguished from gall-stone colic, ureteric colic from labour pains, intercostal neuralgia from angina pectoris, and so on.

On the other hand, we naturally cannot conclude that an unpaired organ is the cause of bilateral hyperalgesia. In pyelitis cases, for example, we frequently see double-sided hyperalgesia, not because the pyelitis is complicated by disease of unpaired organs, but because it is bilateral.

In æsthesioscopic investigations we should remember the blood supply of the organ. If we believe we have to do with uterine disease, for example, and find, in agreement with this, marked bilateral sacro-lumbar reflex anæmia without accompanying epigastric cutaneous anæmia, attention should be directed to other organs which may cause corresponding lumbar anæmia without associated epigastric cutaneous anæmia (e.g., rectum and certain of the aortic segments). But if the actual organ has been detected, and it is further desired to find the segmental level, the fourth rule must be made use of, that is to say, we determine the segmental position of the lower edge, and thus ascertain the place of origin of the pain.

We must remember that many organs may be situated at the same level as regards the afferent segmental innervation. If we find, for instance, reflex anæmia of the shape and position of that shown in *Fig. a-d-e*, we know that it corresponds to that found in cholelithiasis; but high level duodenal diseases, aortic diseases of the same segmental level, and probably pancreatic diseases can cause exactly the same reflex anæmia. On the other hand, if we find it corresponding to *Fig. a-d-g-e*, we can conclude with certainty that the pain is not due to biliary colic, since the reflex anæmia caused by the latter, irrespective of the degree of the pain, does not reach below the line joining the tips of the two 9th ribs (line *d-e*).

The determination of the level is important (1) in the localization of the seat of the pain when diseases of the organs with long lumens are concerned (digestive canal, ureter, aorta), and (2) for identifying the organ itself, since by æsthesioscopy we determine the segmental position of the disease, so that we can discover which organs belong to the zones in question.

As a guide for this purpose the table below is given, which also records the afferent segmental innervation of the organs as determined by the æsthesioscopic findings.

(It must be emphasised that the lower border is the important one. The upper border is less definite, probably because every part of an organ is innervated from more than one segment. Uncomplicated appendicitis is thus frequently accompanied by hyperalgesia spreading over two or three segments, gradually becoming indefinite in a proximal direction, presumably because the tracts are chiefly incorporated in one principal segment, but as the number of fibres decrease they become connected with adjacent segments.)

LOCALIZATION OF THE AFFERENT SEGMENTAL INNERVATION OF THE VARIOUS ORGANS.

Trachea.	.	.	.	3rd dorsal segment to 6th cervical segment.
Bronchi.	.	.	.	6th dorsal segment to 2nd dorsal segment.
Bronchioles	.	.	.	9th dorsal segment to 6th dorsal segment.

Alveoli	12th dorsal segment to 9th dorsal segment.
Distal end of œsophagus	7th dorsal segment to 5th dorsal segment.
Stomach	8th dorsal segment to 6th dorsal segment.
Biliary passages	9th—8th dorsal segment to 7th—6th dorsal segment.
Small intestine	11th dorsal segment to 9th dorsal segment.
Ascending, transverse and descending colon	12th dorsal segment to 10th dorsal segment + 8th to 6th dorsal segment.
Sigmoid flexure	3rd lumbar segment to 12th dorsal segment.
Rectum	5th sacral segment to 12th dorsal segment.
Prostate	2nd—1st sacral segment to 12th dorsal segment + 9th to 6th dorsal segment.
Uterus	2nd—1st sacral segment to 12th dorsal segment + 9th to 6th dorsal segment.
Fallopian tubes	1st lumbar segment to 12th—11th dorsal segment + 9th to 6th dorsal segment.
Heart	7th dorsal segment to 4th dorsal segment.
Aortic arch	2nd dorsal segment to 6th cervical segment.
Cœliac artery	9th dorsal segment to 6th dorsal segment.
Superior mesenteric artery	12th dorsal segment to 10th dorsal segment.
Inferior mesenteric artery	3rd lumbar segment to 11th dorsal segment.
Spermatic artery	9th dorsal segment to 7th dorsal segment.

(As the 4th cervical segment to the 2nd dorsal and the 1st lumbar segment to the 5th sacral are not represented in front, or at any rate only by rudimentary zones, the determinations in the case of these segments are made from observations of reflex anæmia on the back.)

These are the chief facts we must bear in mind when we wish to determine the seat and origin of visceral pain from a study of viscerocutaneous reflex anæmia. It must be emphasized that these investigations are only applicable to localization; they reveal nothing of the *nature* of the causative disease. Applied with discretion, the method can undoubtedly yield more reliable information about the seat of visceral pain than any method of sensory investigation hitherto used, because the principle of the method is to observe and interpret the affected organ's own sensibility, expressed as it is by the viscerocutaneous anæmic zones.