ALIMENTARY TOXAEMIA.

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CUTANEOUS INDICATIONS OF ALIMENTARY TOXAEMIA.

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FROM the days when we were house-physicians, the occurrence of alimentary toxæmia, as the term is understood in this discussion, must have been familiar. Many of us may recollect the occasion when we were called to the casualty department late on a Saturday evening and found awaiting our services a vigorous looking young man, whose features were scarcely recognizable on account of an outburst of severe urticaria. We found on inquiry that his week-end dissipation had been stimulated by a diet of stout and winks, and our judgement as to the cause of the urticaria was supported when we found that the best treatment in such cases was the administration of an emetic, followed by a copious black draught. No doubt remained in our minds that the urticaria was due to alimentary toxæmia, caused by poisons absorbed from his alimentary tract.

In such a case as this the relation in time between the disturbance of the alimentary tract and the visible indication of disease is so close that their causal relationship is admitted by all. But in the case of most other indications of intestinal and visceral disturbance the relationship between the probable cause and its manifestation cannot be so easily traced. Even with the knowledge now at our disposal as to the nature of the poisons derived from various fermentative processes, the chain between cause and effect cannot be distinctly demonstrated; mathematical methods of proof are not applicable, so that all we have to offer in support of our beliefs are the conclusions drawn from individual or collective clinical experience. Nevertheless, little doubt is left in the mind of the clinician that causal relationships do exist, and it may be well to point out at this time some of the more obvious external signs of disease of the alimentary tract.

The poisons capable of producing toxæmia resulting in these manifestations of disease seem to come from two sources: first, those contained in the food itself or arising from the food by the action of ferments in the alimentary tract—these ferments may be those normally produced by the various accessory glands or may have some abnormal origin owing to disease or other causes; secondly, those resulting from fermentative or putrefactive processes due to the action of organisms which may be normal denizens of the alimentary tract or interlopers. Most of the external manifestations seem to be more easily traceable to the first group of poisons rather than to the second, though this may very possibly be due to the fact that the noxious consequences of the action of many of these organisms, such as bacteria, are more difficult to appreciate and to trace to their original source.

The outward manifestations group themselves easily in four main categories:

1. Those resulting from disturbances of the blood vessels which disappear leaving no permanent trace. In this category may be grouped the varieties of urticaria, evanescent or of long duration, the types of erythema, including exudative and vesicating forms.

2. Morbid conditions in which an inflammatory lesion progresses to actual infiltration of the integuments with cellular elements and terminating in persisting deformity such as dilatation of blood vessels, atrophy, persistent dermatitis, ulceration, and scarring.

3. Purpura in its different forms—punctate, diffuse, and often associated with other hæmorrhagic manifestations.

4. Pigmentation due to increase or abnormal distribution of pigments closely related to those of the normal type, such as melanin, or in other cases to pigments more recently derived from hæmoglobin and due to hæmolysis resulting from the circulating intestinal toxins.

GROUP I.

Of the first group, the various forms of simple or acute urticaria are by far the most common. The relationship between the ingestion of an unusual article of food such as shellfish or certain fruits, with the consequent outburst of urticaria, is so close as to leave no reasonable doubt that the poisonous material is contained in the ingested substance, or is very easily elaborated from it by the digestive ferments. A little more difficulty is felt when dealing with other varieties of the disease, such as the recurring type of urticaria, in which the lesions are usually not so severe or extensive as in the acute single attack, or the chronic variety, in which the lesions are usually diffusely scattered, though not large individually and leave indurated lesions, giving rise to the term "papular urticaria." These papules not infrequently develop long-standing pigmentation, and may even resemble the rare condition known as "urticaria pigmentosa," of which the exact morbid relationships are still unknown.

In reference to the causation of these less common types of urticaria, the connexion between ingested poisons and the production of the lesion is not so easily traceable, but information gathered from clinical investigation strongly indicates the existence of the connecting chain. For instance, in one case it may be discovered that some individual article of food little suspected to be the cause has by a process of elimination been at length excluded from the dietary. As soon as the sufferer denies himself this treasured delicacy, the troublesome and long-standing urticaria disappears. Also, although the treatment of the chronic and papular varieties of the disease is by no means satisfactory, and often very disappointing in its results, the largest amount of success follows treatment by careful selection of the diet—sometimes by restriction of proteins, at other time by refraining from carbohydrates, accompanied by treatment adapted to keep the alimentary canal in a healthy state.

The relation between the various forms of erythema and alimentary toxæmia is more obscure. That such a relation does exist is borne out by the clinical experience of the causation of some of the simpler forms of erythematous eruption.

Take, for example, the simpler types of non-exudative erythema. It is well known that such outbreaks are apt to occur after the disturbance of the lower bowel and its contents by the administration of injections, or as a consequence of lavage of the rectum and colon. The cause in this case is not likely to be due to absorption of the fluid used for purposes of washing out the bowel, but to substances pre-existing in the alimentary tract, or rapidly formed in consequence of the interference with its contents. The material absorbed into the body producing attacks of erythema in cases such as these may, with some degree of likelihood, be ascribed to the effects of bacterial decomposition. No doubt, at any rate, exists in our minds as to the causal relationship of the erythema and the administration of the injection. It is reasonable, therefore, to suspect that other conditions of the large intestine, such as those produced by disease of the mucous membrane, may manifest themselves by erythematous eruptions on the surface, and as a matter of observation simple erythematous eruptions are by no means infrequent in the course of the various forms of inflammation of the bowel. These outbreaks are very apt to be purpuric.

The types of erythema exudativum in which, in addition to dilatation of the capillaries, escape of the contents of the vessels occurs into the tissues—either the blood serum or the blood cells—are by far less common than the simple erythemas. We are less likely, therefore, to observe the association between eruptions of erythema exudativum and affections of the alimentary tract, but that the relationship does exist in many cases is more than probable. The close connexion between outbreaks of exudative erythema and diseases of internal organs has frequently been noted and emphasized by various writers, and the toxæmia producing these attacks may arise with greater probability from the alimentary canal than from other viscera. Instructive examples are quoted by Osler and other observers.

The general impression given by clinical observation of this group of external manifestations is that the urticarial type is more frequently produced by the direct absorption of noxious ingesta or as a consequence of the more simple

chemical changes in foods occurring in the upper portion of the alimentary tract from the action of the natural alimentary ferments; while eruptions of erythematous nature more frequently arise from affections of the intestines, especially the large intestine, in which the terminal processes of digestion take place, the poisonous materials involved being of a more subtle character, or perhaps due to the results of fermentations produced by bacteria or other organisms. The purpuric types of erythema seem especially to indicate that the changes occur in the colon or large intestine.

GROUP II.

The external lesions which we have been considering are those due to vascular phenomena, which leave no permanent trace behind. Closely allied to these lesions are certain others in which, in addition to the erythematous condition, tissue changes occur. Of these the criterion is the appearance of new cellular elements—neither red blood cells nor white blood cells, but newly formed cells, characteristic of various types of inflammatory infiltration. When these new cells are observed destructive tissue changes must occur in some degree, though it may be very slight, and as a result we may observe erythematous lesions with the same symmetrical disposition as some of the others we have discussed, but which do not vanish, leaving as their result atrophic, or even ulcerating, destruction of the surface. The type of this morbid state is the disease usually known as lupus erythematosus—a condition closely resembling in its distribution erythema multiforme, but terminating in some degree of destruction or atrophy. The etiology of this mysterious affection is by no means well understood, but its connexions with visceral disturbances should never be overlooked. A good deal of attention has been drawn to its peculiar relationship with certain forms of disease of the kidney. In other cases a poison arising from the alimentary tract may be suspected of being the cause. A characteristic example is as follows:

A woman of about 35 years of age came under observation with an acute outburst of lupus erythematosus affecting symmetrically not only the face but also the extremities and the trunk, accompanied by fever and much constitutional disturbance, resembling, therefore, the well-known type of the disease sometimes called "exanthematic lupus erythematosus." The duration of this case was about three years. The investigation into the possible causes of the disease were at first unfruitful, but soon it was noted that the patient was gradually developing the signs and symptoms of cirrhosis of the liver. It was not, however, till well on in the course of her malady that it became known that the patient, who in all other respects was exemplary in her social behaviour, secretly indulged in alcohol to an excessive degree.

Such cases occurring in the course of medical experience naturally give rise to the belief, and indicate with a good deal of certainty, that certain forms of alimentary toxæmia may result not only in such conditions as hepatic cirrhosis or fibrosis of the kidneys, but also in the outward and visible sign of a chronic inflammatory erythema, ending in induration or atrophy of the skin. In this relationship notice should be taken of numerous cases in which permanent dilatation of blood vessels results in the production of the different clinical types of telangiectases or even of angiomas. A good deal of attention has recently been given to the different forms of these permanent vascular lesions. Some of them seem to occur almost certainly as the result of circulating poisons affecting the blood vessels mainly. They are frequently seen in cases in which cirrhosis of the liver and kidneys have followed toxæmia arising in the first instance from the alimentary canal.

GROUP III.

The probability of alimentary toxæmia being the cause of certain cases of purpura has long been recognized clinically, for the connexion between the outburst of purpura and the disturbance of the alimentary canal is sometimes so close that it gives as clear evidence of their relationship as the outburst of urticaria following the eating of some unusual article of food. This relationship is well seen in some of the cases producing the type of the disease known as Henoch's purpura. Many purpuric

lesions arise no doubt by a peculiar development or simply by intensification of the conditions already noted producing erythema. They form, however, on account of their aspect so characteristic a group that they claim special attention.

One of the most remarkable conditions in which the connexion between poisoning from the alimentary tract and the outburst of purpura is shown is in certain stages of hepatic cirrhosis. In these cases of cirrhosis, sometimes at an early period of the disease, a patient is attacked by a violent outbreak of purpura, the lesions occurring throughout the body affecting large areas and showing profuse extravasation of blood. These outbreaks are often associated with internal hæmorrhages most commonly from the lower part of the bowel. Such attacks of purpura seem to occur in the early stages of obstruction to the portal circulation caused by the contracting of the newly formed connective tissue in the liver. As a result the portal blood containing the crude materials absorbed in the alimentary canal is forced to seek collateral channels to regain the general systemic circulation. Much of it returns directly by means of the vena cava, thus closely reproducing the conditions established by the well-known porta-caval fistula of Eck. The blood returning by these newly formed channels of circulation carries with it the products of intestinal digestion, or possibly abnormal noxious substances due to the impaired action of the alimentary canal. Under normal conditions the liver is the organ in which these materials are further elaborated, thereby being rendered innocuous, or are destroyed, but in the unusual conditions produced by portal obstruction the tissues, the blood vessels, and the blood itself are poisoned for the time being. It is under these circumstances that certain exceedingly violent attacks of purpura arise, and they strongly suggest the causation indicated. It is not surprising to find that hæmorrhages from the bowel are associated with these purpuric outbreaks. New channels are being discovered by the returning blood, such as those uniting the superior and inferior hæmorrhoidal vessels and the radicles of the internal iliac vein; extravasation is likely to occur under these circumstances from the dilated blood vessels quite apart from the noxious effects produced on the tissues by the abnormal constituents of the blood. In such a case the attack of purpura may be the first indication drawing attention to the visceral and intestinal disease. Complete recovery of the hæmorrhagic symptoms may occur, the patient being even able to resume his usual work in life. The cirrhosis of the liver, of course, remains, or gradually progresses, but the gland apparently resumes its functions as the purifying organ of the portal blood to a sufficient extent to protect the body, or the tissues of the body succeed in protecting themselves in some other way against the action of the poisoned blood. It is likely that the poisonous materials producing these changes in the tissues and in the blood are the results of the ordinary digestive processes or the simpler forms of chemical decomposition rather than of bacterial fermentations.

Another variety of purpura presents small hæmorrhagic areas of petechial or punctiform lesions. The relationship between this condition and alimentary toxæmia is very distinctly shown in the variety of disease to which the name of "Henoch's purpura" has been given. An instructive example occurred in the case of a young girl, who presented herself for treatment two or three years in succession with attacks of intestinal pain, melaena, hæmaturia, and numerous purpuric lesions. On every occasion the attack followed an autumn visit to the country, and the eating of unusual foods, such as berries and nuts.

The same type of purpura is very familiar in association with chronic inflammatory conditions of the colon, such as the varieties of colitis and dysentery. The attacks are especially prone to appear when other evidences of toxæmia or septicaemia become prominent.

There are grounds for associating the type of purpura characterized by large areas of cutaneous hæmorrhage with absorption of poisons from the upper part of the alimentary tract. These poisons may arise from infected food materials or may be produced by the normal, or only slightly abnormal, processes of intestinal digestion. The petechial and punctiform types of purpura, on the other hand, appear to occur as the result of the terminal

digestive changes or abnormal fermentative processes occurring in the lower reaches of the bowel, possibly influenced by the micro-organisms present in the alimentary tract. This is the type of purpura most often seen in cases of severe septicaemia which seem to be traceable to the pyogenic inflammations of the mouth, gums, or naso-pharynx.

GROUP IV.

A fourth group of the visible manifestations of alimentary toxæmia includes the abnormalities of pigmentation. The unhealthy, dusky discoloration of the skin occurring in various forms of indigestion is a matter of ordinary observation. Much attention has been drawn in the course of this discussion to the discoloration occurring in the cases of disease to which the name of "intestinal stasis" has been applied. It is difficult to be quite sure of the exact nature of this pigmentation. It is partly due, no doubt, to disturbances of the circulation, producing unusual conditions of opacity or translucency of the skin, but in other cases, no doubt, it is due to a definite increase in the amount of the pigments, identical with, or nearly related to, the normal skin pigment. The cases, however, which are most striking are those in which the pigmentation is due to unusual or abnormal pigments.

The first to which reference should be made is the peculiar yellow tint, probably resulting from severe hæmolysis, followed by liberation of hæmoglobin in the blood serum, and the formation of pigments, of which urobilin is one. This hæmolytic, or "urobilin jaundice," as it is sometimes called, is well seen in the severer forms of anaemia, many of which are associated with septic disorders of the alimentary tract; the poisoning in these cases, giving rise, as one of its consequences, to abnormal hæmolysis, is probably of bacterial origin. It is very usual to find these hæmolytic changes associated with obvious purpuric lesions.

The most striking of all the varieties of abnormal pigmentation is seen in the cases to which the name of "hæmochromatosis" is given. The pigment in this condition is not so close a blood derivative as is urobilin, and probably more than one variety of pigment may be present. Of these a pigment still containing iron has been identified with some certainty, to which the name of "hæmosiderin" has been given, while another pigment free of iron is known as "hæmofuscin." The staining and discoloration of the tissues resulting from the formation and disposition of such pigments is often of a most remarkable character. In some cases it is of a pronounced slate-black colour, while in others the tint is a full mahogany brown. There can be no doubt also that the depth of the pigmentation may vary from time to time in the same case. The relationship between some of these cases of hæmochromatosis with poisoning arising from the alimentary tract is very close. Cases are on record in which inflammatory conditions involving the abdomen and interfering with the action of the intestine have coincided with the development of the slate-black pigmentation already mentioned. The discoloration may show itself on the surface of the body in a degree which can scarcely be imagined unless the opportunity has arisen of seeing such a case. In one such case recovery from disease affecting the intestine following operation was accompanied by the gradual disappearance of discoloration of the most intense character. This patient was well, in vigorous occupation and health, several years after treatment.

On the other hand, the type of disease associated with enlargement of the spleen, progressive loss of health, with severe anaemia and frequently with repeated discharges of blood from the bowel, and in which cirrhosis of the liver occurs as a terminal feature, shows pigmentation of the red-brown tint. In a case presenting these features the pigmentation of the surface was of a pronounced mahogany-red colour.

In this category may also be included the cases of discoloration due to alterations in the hæmoglobin to which the names of "methaemoglobinaemia" and "sulphaemoglobinaemia" have been applied.

In many of these abnormal pigmentations the relationship to alimentary toxæmia is a close one—probably that of cause and effect.

CHRONIC INTESTINAL STASIS.

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As my contribution to this discussion I propose to examine the evidence on which a diagnosis of toxæmia due to chronic intestinal stasis can be made. It might be gathered from what some clinicians have said that it is possible to make a diagnosis from the symptoms alone. If, for example, we could accept the statement that chronic intestinal stasis is "a necessary antecedent factor" in the development of all forms of tuberculous disease, the discovery of tubercle bacilli in the sputum would logically lead to a diagnosis of chronic intestinal stasis. Few, however, will agree with a statement for which so little evidence has been brought forward. Even the symptoms, which are by common consent regarded as characteristic of chronic intestinal stasis, are by no means pathognomonic. The worst case I have ever seen of intestinal toxæmia, in which the classical symptoms of extreme emaciation, extensive pigmentation, evil-smelling sweat, and cold extremities were present, was due not to chronic intestinal stasis but to chronic diarrhoea, the result of some intestinal infection, contracted by a lady whilst big game hunting in West Africa.

It is not at all uncommon to be told by a patient, who is in the habit of taking large quantities of aperients for constipation, that the lassitude, headache, and abdominal discomfort from which he suffers are better if he forgets to take his aperient and his bowels are not opened. His symptoms appear to be due to the absorption of poisons from the abnormally fluid faeces in his colon, and are therefore a result of the diarrhoea produced by his aperient, and not a result of his constipation. It is important before examining such cases with the *x* rays that the patient should not take any aperient for some days. When this has been done, I have often been able to demonstrate the complete absence of intestinal stasis, although many of the patients were contemplating some operation for relief of their supposed constipation. The bismuth reached the rectum in the normal time, but the patients had become so convinced that their bowels would not act without help that they made no attempt to open them, as they did not feel the violent desire which resulted from the use of their aperients. When it was explained to them what the *x* rays had shown, and also that a finger inserted into the rectum proved that it was full of faeces only waiting to be expelled, they were persuaded to try to open their bowels, and succeeded in doing so. A gentleman, 38 years old, whom I saw in April, 1910, was convinced in this way, and he has had his bowels opened regularly ever since without treatment of any sort, although up to that time he was taking an enormous quantity of aperients, and was sent to see me for an opinion as to whether the colectomy which had been advised ought to be performed.

It is well known that the frequency of the stools gives no certain evidence as to the existence of intestinal stasis. Thus a condition analogous to retention of urine with overflow may occur in the bowel, the patient being exceedingly constipated, but passing numerous small stools every day. On the other hand, in the condition aptly described as "greedy colon" by Sir James Goodhart, the patient may only open his bowels once every three or four days, and yet be perfectly healthy; in such cases I have found with the *x* rays that the passage through the bowels is generally normal in rate, but the quantity of faeces formed is so small that several days may be required for sufficient to collect in the pelvic colon to give rise on entering the rectum to the call to defaecation.

By giving some charcoal with breakfast one morning, and watching for its appearance in the stools, the total time taken in its passage through the alimentary canal can be ascertained; but this method gives no indication as to the part of the bowel in which stasis occurs.

We are therefore driven to the conclusion that the only reliable means of determining whether a patient is suffering from chronic intestinal stasis and of ascertaining