—probably by diffusion—raise the osmotic pressure of the lymph, and attract water from the blood. In this way the increased lymph flow is accounted for. It is, of course, possible that bile salt (and haemoglobin) stimulate the hepatic capillaries to secrete lymph, after the manner suggested by Heidenhain. But the experiments, though not actually opposed to such a view, do not support it.

REMARKS ON A CASE OF HEREDITARY LOCALIZED OEDEMA PROVING FATAL BY LARYNGEAL OBSTRUCTION.*

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DURING the last sixteen years I have had under my observation from time to time some remarkable cases of localized oedema, and I will give the history of one of the cases which was the most striking I have ever seen, and will append some general considerations on the subject.

History of the Case.

The patient was a young woman, aged 18 years, when she first came under my observation. She was admitted into the infirmary under the care of Dr. Eddison on June 21st, 1886, with great oedema of the right arm and hand, and was suffering from dyspnoea. Her voice was husky, and she had some pain on swallowing. Her tongue was coated, but her general health was good and there was no albuminuria, and it was the difficulty in breathing which determined her admission. On laryngoscopic examination there was found very great oedema of the mucous membrane covering the epiglottis and aryteno-epiglottidean folds, so great as almost entirely to conceal the vocal cords. The question of tracheotomy was considered, as was also that of scarification of the swollen mucosa, but it was deemed safe to wait. By the evening the oedema had entirely disappeared from the larynx, the swelling of the arm rapidly subsided, and she was discharged well at the end of five days.

From the patient and her mother the following interesting history was subsequently elicited. Ever since infancy she had been subject to localized swellings on various parts of the surface of the body. Thus shortly after birth one arm swelled to such an extent that the clothing had to be cut to release it. Very often she used to notice a small rounded swelling like a marble under the skin which would enlarge and become diffuse, so that the skin, say on the back of the hand, would swell enormously, and swellings more or less diffused or localized used to develop with great rapidity on her hands, feet, shoulders, chest, or around the vulva. Sometimes these were attended with slight redness and tickling, and when the vulva was affected, micturition was painful but not difficult. These swellings came on with great frequency, but no periodicity had been noticed. Menstruation had been established at the age of 15, and had always been normal, and apparently without influence on the incidence of the swellings. She was unmarried, but had had one child.

A careful examination of the patient failed to reveal any signs of disease or constitutional disturbance of any kind, except that for many years she had been subject to what she termed bilious attacks.

Her father from his earliest infancy had presented swellings of the same kind. On three occasions these seem to have affected the throat. The first attack of this kind occurred at the age of 21, the second a few years subsequently, and the third attack carried him off at the age of 29. He had come home from his work saying his throat was getting swollen, and his medical man who was sent for went to get something for his relief, but during his absence he suddenly got blue in the face and died asphyxiated.

From 1886 the patient was frequently seen by me at intervals until her death within the last few weeks, and I had frequent opportunities of seeing the remarkable swellings. They were, as she described, diffuse or circumscribed. Usually pale, but sometimes slightly pink, they did not pit

on pressure, and I never found that they became vesicular or bullous.

On two occasions the symptoms were rather alarming, and deserve special notice. In July, 1890, she struck her head against the lock of a door, which made her feel sick and caused a small lump on the forehead. Next day the swelling had passed down, affecting the eyelids and the face, and the following morning, when the swelling of the face was beginning to subside, her throat became slightly affected, and felt, she said, as if something were sticking in it. When I saw her, her face was much swollen, the swelling stopped at the margin of the hairy scalp and at the ears, and did not extend on to the neck. In a short time her appearance was again perfectly normal.

In October, 1891, she complained of slight toothache one day, with swelling of the same side of the face. During the night, and especially during the following day, the swelling rapidly increased, and then her voice became affected. At 11 o'clock at night I found her sitting up, in which position the dyspnoea was more tolerable, with her face swollen out of all possible recognition, and presenting the general aspect of a patient with acute renal dropsy of an extreme character. The oedema was practically confined to the face and under aspect of the chin; it was firm, did not pit readily on pressure, and somewhat resembled that of myxoedema, though much more pronounced than anything I have ever seen in that affection. The tongue was swollen, as was also the mucous membrane of the mouth, and the lips were so swollen that the mouth naturally remained slightly open, and the continual escape of the buccal secretion led to a constant necessity for mopping the mouth. The larynx was readily examined, but all that could be seen were three rounded masses, pale, jelly-like, and tense, representing the swollen mucous membrane covering the epiglottis and the two arytenoid cartilages, while the false and true cords were completely concealed. The voice was not much affected. Next day she was much better, the voice was clear and the swelling of the face was manifestly subsiding. The following morning she was perfectly well, nearly all swelling had gone, and the larynx was absolutely normal. A slight feeling of sickness during the night was the only manifestation she had had of general disturbance. The bowels were normal, and there was no alteration in the amount of urine passed.

Some six or seven years ago the patient was married and had three children. Her pregnancies, as on the former occasion, had no influence on the occurrence of the swellings.

The patient was fully alive to the risks attendant on the attacks of swelling in the throat, and the final scene justified her apprehensions. On February 20th, 1902, at 10.30 a.m., she mentioned to her mother that her throat felt swollen, but that the swelling seemed to be passing backwards, and she thought she would soon be all right again. At noon her husband came home from his work, and found her sitting on the floor to all appearance comfortable and free from dyspnoea, and amusing her child, for whom she was just going to spin a humming top. Suddenly she dropped the top, started up, apparently tried to speak, clutched at her own neck, and then at the throat of her husband, which I take to have been a pantomimic action expressive of her distress; got blue in the face, and died almost at once. When I saw her, in about half an hour, the features were livid, the tongue was very slightly protruded between the teeth, and there was some fullness about the neck. Her mother, who had left the room, had again arrived on the scene just at the moment of death, and her first words to me were that her daughter had died in exactly the same way as her father before her.

Necropsy.

The necropsy I made was an incomplete one, but I removed the larynx by cutting widely beyond its limits, and with as little disturbance as possible. The mucous membrane was very oedematous, tense, and pale, and the sides of the laryngeal cavity came in contact with one another a short distance below its superior aperture, and remained so until just below the level of the true cords. A small amount of viscid mucus was found in the cleft between the two opposed mucous surfaces, which may have possibly assisted to a very slight degree in the occlusion, but the oedema was so great that it is not necessary to invoke any such considerations. I

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can readily understand that even with a rapidly increasing oedema placid respiration might go on; but when the occlusion was getting almost complete any sudden inspiratory effort, such as might accompany a sudden turning or change of position on hearing her husband coming, might be the determining factor in causing the occlusion by sucking together the greatly swollen walls of the larynx.

A series of transverse sections of the larynx proved very instructive, for it showed that the oedema affected not only the mucous membrane but the deeper connective tissue, and even the substance of the muscles, which latter condition would, I think, prevent the abductors from causing that physiological enlargement of the aperture during inspiration which is so important in ordinary respiration. The oedematous fluid was purely of the serous variety, untinged with the colouring matter of the blood; and, contrary to what is usually stated to be found in oedema of the larynx, the tissue covering the true vocal cords was decidedly affected.

Commentary.

One of the most valuable contributions to the subject of angeioneurotic oedema was that of Osler in 1888 who emphasized the association with the swellings of symptoms of gastrointestinal irritation and gave a striking example of the influence of heredity, an influence which had been formerly pointed out by Quincke, Strübing and Falcone, for he was able to trace the disease through five generations in one family, no fewer than 22 members having been affected, and of these 1, if not 2, died of an active oedema of the larynx.

The attention of the profession was, I believe, first called to this affection as a definite entity in 1882 by Quincke who gave it the name of acute circumscribed oedema of the skin. Cases had indeed been formerly described by Sir Thomas Watson, and under the name of fugitive oedema by Laycock, but to Quincke is due the credit of suggesting the view which is now held by most that the oedema depends upon a condition of altered innervation of the part, and Strübing's term of angeioneurotic oedema implies his acceptance of this theory. By some the swellings have been referred to as "ephemeral congestive tumours," the term "wandering oedema" is purely descriptive and embodies no kind of theory, while the least committal of all is employed by Dr. Landon, of Ebling, who describes the condition simply as "a peculiar skin disease." The terms "massive" urticaria (Rapin) or "giant" urticaria (Milton) express a theory as to its causation and relations, which is quite in harmony, of course, either with the views of Quincke and Strübing, or with the view that the condition is due to some kind of toxæmia, and I think there can be little doubt but that the affection really is of the nature of an urticaria or an exudative erythema, for between typical examples of the two affections there is not any sharp line of division.

The influence of the nervous system on the production and determination of the situation of dropsy is far reaching and important. A familiar example is afforded by the classical experiment of Ranvier, which, however, appears to be in antagonism with those of Lower, performed 230 years ago. Ranvier ligatured the chief vein in the limb of a dog without causing oedema, which however promptly developed when the sciatic nerve was cut. Section of the lingual nerve, with irritation of its peripheral portion, according to Cohnheim's experiment, causes oedema of the tongue in the frog. Injury to nerve trunks and cervico-brachial neuralgia has resulted in oedema in the human subject, and Gowers notes the association of trigeminal neuralgia with venous distension on the same side, and with oedema of the scalp. Charcot called attention to the association of oedema with hysterical palsy of a limb, the oedema vanishing with the return of power. The rapid effusion into the joints in tabetic arthropathy is a good example of dropsy due to nervous influence, and especially interesting in this connexion, for in one of Quincke's cases of circumscribed cutaneous oedema repeated effusions occurred into the articulations. Leyden has described oedema as occurring in spinal myelitis, while in alcoholic paralysis it is a familiar phenomenon in the acute stage. The most marked example I have ever seen of dermatographia, which is, of course, a traumatic urticaria, and therefore an oedema, was in an alcoholic subject convalescent from pneumonia. In hemiplegics who from any cause, cardiac or renal, develop dropsy I have repeatedly noticed that the oedema is

more marked on the paralysed side. Crocker had a patient in whom urticaria always developed on the advent of a stranger, and as urticaria is clearly vasomotor in origin, this is in harmony with the flushings, pallors, and blushings of mental emotion.

Localized oedema has been frequently noticed in connexion with many conditions. I may mention that found in rheumatoid arthritis, the oedema on the dorsal aspect of the hands in tetany and in rickets, and the whole class of erythemas and oedemas due to certain drugs, such as arsenic, belladonna, and potassium iodide, to the use of which drug Fournier attributes two instances of sudden death from oedema of the larynx; and, as we are here dealing with poisons, I may mention the enormous swelling that occurs in some people from the bites of certain insects, while we know that extensive localized oedema is not uncommon in those the subject of gout, apart, of course, I mean, from that which accompanies obvious articular inflammation.

Dr. Allan Jamieson records an instance of very acute pulmonary oedema in a young woman of 19, coming on with dramatic suddenness on exposure to a chill after exertion, putting her life in imminent danger, but passing off with great rapidity, and which he very correctly, I think, comments on as analogous with the cases described by Quincke.

I am very far from wishing in this paper to enter upon a discussion of the causation of dropsies in general, but in considering the nature of this remarkable form of oedema of which I have given you an example, we must see that, characterized as it is by irregularity of distribution, by possessing at least in its earlier stages a margin which may be singularly abrupt, and by its rapidity of onset and decline, it differs from the dropsies of cardiac and hepatic disease, which are usually regarded as more purely mechanical in causation, and in a lesser degree from the dropsy of renal disease.

I am, however, by no means sure that this so-called angeioneurotic oedema differs *toto coelo* from that of renal or even of cardiac and hepatic disease. The cause of renal dropsy is eminently obscure; the general anasarca, which my surgical colleagues tell me follows sometimes on colossal transfusions, would seem to me to indicate that a hydraemic condition of the blood is favourable to its development, a view which I think is now becoming discarded in favour of that which adopts the term toxæmia as its watchword, and certainly this latter view is strengthened by the analogies of drug dropsies, such as that caused by potassium iodide.

Even the ascites of hepatic disease and the dropsy of cardiac disease are not susceptible of a purely mechanical explanation. Hale White has shown that the recurring ascites of cirrhosis is usually associated with chronic peritonitis, and to this rather than to the liver disease he attributes the effusion. I am not aware that the back pressure of mitral stenosis is less than that occurring in mitral regurgitation. The great hepatic fullness and the tendency to pulmonary hæmorrhage would seem to indicate that it is not so; yet dropsy is much more common in mitral regurgitation than in mitral stenosis, and the dropsy of primary cardiac muscular failure such as is seen in alcoholic paralysis seems to be regulated so little by the laws of gravity that its explanation must be different from that which is applicable in cases of valvular disease with failing compensation.

While, therefore, on the one hand, I hold that these cases of localized oedema such as I have described constitute a class sufficiently definite to entitle them to a special description, I cannot but feel, on the other hand, that when the conditions which determine the occurrence of dropsy in rheumatoid arthritis and gout, in association with lesions of the nervous system, under the use of certain drugs, in acute renal disease, or on exposure to cold without evidence of renal involvement, and even that in cases of cardiac and hepatic disease, which is susceptible of a more purely but not as I think of an altogether mechanical explanation, are fully understood, the relationship between this form of dropsy and all the others to which I have referred will be found to be even more intimate than I have ventured to imply.

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