

against fermentative processes in the early stages of the treatment, as indicated. It is of the highest importance to increase the strength of the abdominal muscles by regulated exercise. Belts, or abdominal supporters, so highly recommended and in such variety, are of doubtful utility. Only those belts which increase the intra-abdominal pressure should be used. They encircle the abdomen and exercise the same degree of pressure over the whole abdominal surface. It is not only futile, but often harmful, to attempt to hold a kidney or a stomach in place by any special device externally applied.

With respect to surgical treatment of this condition, it must be said that it should be undertaken only after other methods have failed, and then only with the greatest care, especially in those cases in which the neurasthenic element is strongly manifest, for such patients are often worse rather than better after surgical interference. Duret first operated in 1894, lifting the stomach and fixing the serosa of the lesser curvature of the stomach to the parietal peritoneum and muscle of the anterior wall of the abdomen. Byron D. Davis (1897), Beyea (1898), Hartmann (1899), Treves, Bier, and Webster, have operated with varied success on similar cases. Beyea and Stengel shortened the gastric hepatic omentum and gastrophrenic ligament by plicating with multiple sutures, thus bringing the stomach up to its normal position. Webster, selecting those cases in which there was separation of the recti muscles, sought to increase intra-abdominal pressure by resecting the fascia of these muscles and then suturing the muscles together.

William Fawcett Hamilton.

## LITERATURE.

- Arnell: American Journal of Medical Sciences, April, 1901.  
Duret: Revue de Chirurgie, p. 421, 1896.  
Einhorn: Medical News, September, 1896.—Diseases of the Stomach, 1896.  
Ewald: Diseases of the Stomach, Manges, 1897.  
Fitz and Wood: Practice of Medicine, second edition.  
Feilner: Münch. med. Wochenschrift, 1895.  
Francine: Philadelphia Medical Journal, p. 27, January, 1903.  
Glénard: Lyon médicale, 1885.—Revue de Médecine, p. 75, 1887.—Entéroptose et Neurasthénie. Soc. Méd. des Hôpitaux, Paris, 1886.  
Hamilton: Montreal Med. Journ., September, 1899.  
Hufschmidt: Wien. klin. Wochenschrift, No. 52, 1892.  
Hutchinson: The Practitioner, p. 186, February, 1902.  
Jones and Clinch: Edinburgh Med. Journ., November, 1899.  
Keith: Lancet, London, March 7th, p. 14, 1903.  
Kuttner and Dyer: Berlin. klin. Wochenschrift, 1897.  
Langerhans: Leipzig, Ueber Entéroptose. Monatschrift f. Geburts-hilfe u. Gynäkologie, Bd. viii.  
Leo: Gastroptose u. Chlorose. Deutsche med. Wochenschrift, 1896.  
McPhedran: American Medicine, April, 1900.  
Meinert: Volkmann's Samml. klin. Vorträge, Nos. 115, 116, 1895.—Gastroptose u. Chlorose. Deutsche med. Wochenschrift, 1896.—On Stiller's Sign. Wien. klin. Wochenschrift, June, 1900.  
Osler: Practice of Medicine, fourth edition.  
Putnam: Boston Med. and Surg. Journ., November, 1898.  
Riegel: Diseases of the Stomach, English translation, 1903.  
Rostoski: Münch. med. Wochenschrift, No. 40, 1900.  
Schwerdt: Münch. med. Wochenschrift, November 1st, 1898.—Entéroptose u. intra-abdominale Druck. Deutsche med. Woch., 1899.  
Stengel and Beyea: The Amer. Journ. of Med. Sciences, June, 1899.  
Steele: Philadelphia Med. Journ., p. 174, 1902.  
Steele and Francine: Journ. of Amer. Med. Assn., vol. xxxix., p. 1173.  
Stiller: Archiv f. Verdauungskrankh., Bd. ii., S. 285; Bd. vii., Hft. 4 u. 5.  
Stone: Boston Med. and Surg. Journ., May, 1899.  
Treves: British Medical Journ., 1896.—Allbutt's System of Medicine, vol. iii.  
Taylor: Philadelphia Med. Journ., p. 75, January, 1903.  
Zweig: Archiv f. Verdauungskrankh., Bd. vii., 3.

**ERYTHROL TETRANITRATE**,  $C_6H_6(ONO_2)_4$ , is obtained by the action of nitric acid on the tetratomic alcohol, erythrite, a substance found in several different lichens, especially *Rocella*. It occurs in colorless lamellae, melts at  $61^\circ C.$  ( $142^\circ F.$ ), is insoluble in water, and dissolves readily in alcohol and ether. On percussion or when rapidly heated it explodes with great violence, and one fatality has occurred from its trituration with sugar of milk. In direct sunlight it turns yellow and gives off nitrous fumes.

The drug is a vaso-dilator, and its action differs from that of amyl nitrite and nitroglycerin in no essential except that it is slower in its onset and more lasting. It is said to take half an hour for the production of vaso-dila-

tion, and several hours for the effect to wear off. The dose is gr.  $\frac{1}{4}$ -i. (0.015-0.06 gm.), most conveniently administered in tablet triturates. Bradbury recommends 3 i. (4 c.c.) of a 1 in 60 alcoholic solution repeated every four to six hours. W. A. Bastedo.

**ERYTHROMELALGIA**.—This affection was originally described by Weir Mitchell in 1872 as follows: "A chronic disease, in which a part or parts—usually one or more extremities—suffer from pain, flushing, and local fever, made far worse if the part hangs down," and writers since then have not been able to agree upon a definition more satisfactory than this descriptive one. Up to the present time about one hundred cases have been reported and discussed by neurologists and pathologists, the questions of its pathogenesis, and of whether the affection is properly a distinct disease or entitled only to be called a group of symptoms, having excited much interest. To these topics we shall return in their proper place.

The subjects of erythromelalgia are usually middle-aged people, sometimes young adults, but seldom children. Many more males are attacked than females, and the predisposing causes are such as men are more liable to than women, viz.: occasionally traumatism, as from a stone falling upon the foot, exposure to wet and cold, especially when repeated, long standing at fatiguing work, sometimes exceptionally exposure to heat, as in working at a furnace. Also malaria, syphilis, anaemia, alcoholism, hysteria, and dyspeptic states are all believed to stand in a causative relation to it. It is also found associated with various other general diseases, and particularly those of the nervous system. Reynolds mentions one case as coming on suddenly soon after confinement.

**SYMPTOMS**.—The most distinctive and fundamental symptoms are those originally emphasized by Weir Mitchell. He also in his most recent paper on the subject reminds us that the pure type of symptoms should be looked for in the youngest class of patients, for in those who are more advanced in life diseased conditions of the arterial or nervous system may exist independently of erythromelalgia and lead to confusion. The local symptoms involve almost exclusively the peripheral parts of the extremities. The three characteristic symptoms are localized *pain*, *redness*, and *swelling*, suggestive of inflammation and yet to be carefully discriminated from it. The *pain* is apt to be the first abnormality to attract attention, involving most frequently the great toe, the heel, the ball of the foot on its inner or outer side, or the metacarpo-phalangeal articulation, less frequently the upper extremities, or exceptionally other parts. These pains are described as burning, irritating, piercing, and as sometimes of intolerable severity, "as if the part were being destroyed by fire" (Kahane). They are at first occasional, coming on at varying intervals or after special exciting causes; then they become intermittent and then constant, although there are reports of cases in which they finally ceased. The latter part of the day, especially after exhausting labor, hot weather, a hanging position, also motion, all intensify the suffering; while on the other hand cold, either of the weather or of applications, rest, and an elevated position of the affected part give relief. Thus it is quite characteristic for patients when the hands are the seat of the local trouble to carry them crossed upon the chest or raised above the head (Barlow).

The *redness*, which is the second prominent local manifestation, accompanies the pain, and its tint is variously described as fire-red, violet, livid, the latter verging sometimes into a cyanosis. Weir Mitchell calls it rosy red and congestive, and the disease itself has been called *red neuralgia*.

The *swelling* comes on gradually, is localized like the pain and redness, especially about the joints, but is not marked by pitting. It is increased by motion. Nor is it strange that this association of symptoms has in some cases led to a diagnosis of deep-seated inflammation, for

the relief of which incisions have been made, which, however, revealed nothing.

The seizures thus characterized were called by Mitchell "vascular storms." They may last for several hours or may extend to days or weeks, the local feature sometimes extending to parts not originally involved. The seats of attack are sometimes symmetrical, sometimes not. But in addition to the symptoms already mentioned others show themselves, which have been considered not characteristic of erythromelalgia, and which are not constant, but still may be of importance as bearing upon its pathogenesis. Thus Elsner and Barlow speak of hyperidrosis accompanying the paroxysm, of "innumerable droplets of perspiration standing upon the skin at the time of the most acute pain." There may be a condition described as local asphyxia, which may merge into cyanosis. The pulse is often quickened, which, taken in connection with the changes in the circulation, may be an index of more than local vaso-motor disturbances. Lesions of sensibility are frequently present, hyperesthesia and paresthesia most commonly, but are by no means constant enough to be regarded as characteristic of the disease; nor is the motor function often interfered with, the lesions when occasionally encountered in the more advanced cases being present as weakness and paresis. There is sometimes muscular atrophy. Reflex irritability is infrequent. The *trophic* lesions associated with the local manifestations are frequent and multiform. The skin may be either thickened or show changes analogous to the "diffuse idiopathic atrophy of the skin," of dermatologists, as in a case reported by Schütz. There are sometimes pigmentation and oedema, and lumpy alterations of the joints and nails; also rhagades and ulcers may develop. It is also quite common to find nodules or papules on the reddened and painful areas (Kahane). One other symptom which sometimes presents itself is gangrene, considered by some to be a feature of indubitable cases of erythromelalgia, its occurrence depending upon the greater or less severity of the disease (Sachs), and by others as indicating its alliance with Raynaud's disease.

Such, then, are the local changes, which, says Reynolds, are the only symptoms in twenty per cent. of the cases. The disease is essentially chronic and of very gradual development. Barlow refers to one case which lasted for twenty-seven years, the affection limited to the sole of one foot; Elsner to one involving the left index finger only, for sixteen years, amputation of the finger finally relieving all the symptoms.

Interesting as erythromelalgia has proved to neurologists, it is its pathological position which has given rise to the most discussion, for its symptomatology is well recognized and its diagnosis not ordinarily attended with difficulty. Still there have been but few autopsies reported. The opportunity of examining amputated parts has indeed been availed of, but the findings have not led to general agreement as to its pathological anatomy, and Cassirer, writing in 1901, says: "We are still to-day far removed from any certain knowledge of the pathological anatomy of erythromelalgia." Consequently its pathogenesis has not been satisfactorily determined. Nor have the questions whether it is ever an idiopathic disease, or whether it is merely a "symptom complex," associated with various other diseases, been answered conclusively. It would be impossible here to go into the details of this inquiry, and it has seemed best to give as nearly as possible in chronological order the views of the principal authorities, which will at all events show the trend of professional opinion and develop the mooted points.

Weir Mitchell in his earlier publications refrained from any positive expression of opinion as to the origin of the malady, but later (1878) regarded it as "a vaso-motor neurosis, which might occur either independently or in association with spinal or cerebral disease, where some distinct lesions of definite regions might ultimately be discovered." Subsequently he expressed the view that in erythromelalgia a neuritis of the finest nerve twigs may be present. Lewin and Benda, writing in 1894,

most thoroughly discussed all the cases that had been reported up to that time. They classify these cases under three headings: 1st. Erythromelalgia in organic diseases of the central nervous system. 2d. In functional diseases of the central nervous system (neuroses). 3d. As a peripheral affection (neuritis and neuralgia), the latter group embracing half of all the cases. The vaso-motor symptoms are always secondary to the neuralgic pains. In answer to the question whether it is an independent disease, their conclusion is that it is not a disease *sui generis*, but may be associated with various peripheral and central diseases of the nervous system.

In 1895 Eulenburg wrote that he had reasons for "thinking that the starting point of the disease may be found in certain sections of the gray axis of the cord, especially in the posterior and lateral gray substance, and the associated fasciculi," an opinion which has had great weight.

Auerbach in 1897 published a report of the first complete autopsy made on a case of this disease. There was a normal condition of the peripheral nerves and spinal ganglion cells, marked degeneration of numerous radical fasciculi (Wurzelbündel) in the cauda equina, on one side more than the other, belonging to the first or second sacral nerve and the last lumbar nerve. Pronounced ascending degeneration in the cord.

In 1899 Weir Mitchell and Spiller report that in examining an amputated toe from a patient with erythromelalgia there were found a high degree of degeneration of the nerves, which were almost completely converted into connective tissue, also extreme changes in the vessels, thickening of the media, hypertrophy of the intima, and in places complete closure of the lumen of the artery; and on this finding peripheral neuritis was assumed as the basis of the disease. In this article the opinion is still held that certain cases may be due to some form of spinal disease, but the idea of a nerve-end neuritis is urged. These examinations and others give greater definiteness to the discussion of the pathological relations of the central and peripheral organs in the development of the disease. In Dehio's case 4 cm. of the ulnar nerve and an equal length of the ulnar artery were removed just above the wrist for erythromelalgia involving the hand. The little finger improved, but the rest of the hand remained unchanged. Examined under the microscope the piece of the nerve was found normal, but the artery showed marked arteritis of the middle and inner coats and some diminution of the lumen. Barlow indicates three directions in which inquiry as to the pathology should extend: 1st, to the peripheral nerves; 2d, to the brain and cord, especially in regard to the vaso-motor centres; and 3d, to the blood-vessels. He declares that the disease has been generally regarded as a vaso-motor neurosis or paralysis, and concludes that "in the absence of obvious nerve disease to explain the arterio-sclerosis we are led back to the hypothesis that the chief fault lies with the vaso-motor centres and their abnormal efferent vaso-motor impulses leading to dilatation of the vessels and consecutive disease induced thereby. Some peripheral strain or irritation may have been transmitted to the vaso-motor centre as the original cause of the disturbance." He further expresses the belief that probably the change in the vaso-motors starts centrally, especially in the generalized cases of the disease, although it is more reasonable to suppose that in uncomplicated cases the primary change starts at the periphery. The question whether erythromelalgia is an idiopathic affection or should be considered merely a group of symptoms appearing in association with various primary diseases has brought out a diversity of opinion. Collier in 1898 says it is not now regarded so much as an idiopathic disease as a group of symptoms occurring in other affections, and Kahane, writing in 1900, quotes Lewin and Benda, Eulenburg and Levi as holding the same view, and says the conclusion reached in all the larger comprehensive statements about erythromelalgia is that it is no individual disease, but a symptom-complex accompanying various other diseases of the nervous system.

Kahane himself, however, finally gives as his own opinion that it should be ranked among the acropathies, which he defines as those affections which are localized in the peripheral parts of the limbs and as the ultimate basis of which are assumed lesions of a vaso-motor nature. There is great difficulty in determining whether the nerves or the vessels form the starting point, whether we have to do with an irritation of the vaso-dilators or a paralysis of the vaso-constrictors. He says, in conclusion of a long and careful consideration of the question, that there are two points that one can be sure of: 1st, that erythromelalgia belongs clinically to the group of acropathies; 2d, that it is to be referred to a disturbance in the relation between the systems of the nerves and blood-vessels quite without regard to the question whether it is of functional or anatomical, central or peripheral nature. In his conception it is a phase of disease that occurs in one series of cases independently and in another as an attendant phenomenon of other diseases.

Sachs had found the blood-vessels diseased in most cases, but the nerves not in many; the changes in the latter he believed to be secondary. He says erythromelalgia occurs as an independent group of symptoms, even if not an individual disease. In uncomplicated cases it is probably to be referred to disease of the peripheral arteries. The obliterating arteritis may be indirectly connected with central disease, but may be wholly independent of such influences. In 1901, Elsner, on examination of the arteries in cases that he saw, found them the seat of occasional slight thickening of the intima, but the nerves normal. He calls attention to several cases in which gangrene of the extremities occurred. He believes that erythromelalgia cannot at present be defined as a disease *per se*. Cassirer, on the contrary, is constrained to place himself among those who believe the disease to have a certain idiopathic character, while recognizing like others one class of cases of a peripheral and a second of a central origin. Allchin and Saville regard the disease as of vaso-motor origin, probably allied to Raynaud's disease, the former speaking of it as an expression of vaso-motor ataxia. Shaw in 1903 analyzes nine cases and reports the results of the examination of amputated toes in three cases, stating that "vascular change was present in all, mostly an increase in the intima of the arteries and occasionally thrombosis and changes in the inner coat of the veins. The nerves were investigated even to their terminations, and no degeneration was found, nor was there any suggestion of increase of fibrous tissue in the trunk of the nerves." (Compare Mitchell.) He says: "In no case has recent degeneration of nerve fibres been demonstrated, and in not one of the nine cases analyzed was anesthesia ever present." He concludes that erythromelalgia when occurring independently of central nervous change is associated with but one morbid picture, that of local vascular change. Taubert finds erythromelalgia traceable to disease in the lateral and posterior columns of the cervical cord (see Eulenburg and others). Reynolds calls the disease a vaso-motor neurosis, and argues in favor of the theory of primary vaso-motor dilatation of the arteries followed in the way of compensation for this vaso-motor paralysis by thickening of the coats of the arteries so as to narrow the lumen and stream of blood (quoting Delafield, Thoma, and Barlow in support of his views). Starr, sketching the phenomena of the "vascular storm," says: "The dilatation of the arteries in the extremities results in an extreme condition of redness and sensation of heat and pain. After hours of this the extremities may suddenly become cold, pale, or blue and shrivelled up, presenting the appearance of the hands after long soaking in hot water; and this alternation of distention and contraction of the blood-vessels constitutes the symptomatology of the disease. It appears to be a pure vaso-motor neurosis, but it is rarely if ever attended by any trophic disturbances of the skin or nails, such as occur in neuritis, and no pathological observations are at hand to establish the hypothesis that there is a true neuritis of the vaso-motor nerves."

If, therefore, we should venture upon a rough summing

up of the principal pathological features of erythromelalgia as indicated in the preceding brief synopsis of recent authorities we should say that opinion was settling upon the following beliefs: (1) The disease is considered a vaso-motor neurosis (angioneurosis, Oppenheim); (2) the attribution of the group of symptoms to disease of the posterior and lateral spinal gray matter, when it would be called secondary, and to as yet undetermined causes of peripheral origin, where some would call it clinically idiopathic or *sui generis*; (3) its association with the acropathies and sometimes with Raynaud's disease; (4) there is much more evidence connecting the disease locally with alterations of the blood-vessels than of the nerves, but good authorities deny that we are yet in position to pass finally upon its pathology.

The TREATMENT of erythromelalgia can hardly be said to aim with hopefulness at more than the alleviation of some of its most distressing symptoms, proof of which is found in the long list of the various means employed. Weir Mitchell's recommendation of rest, cold, and elevation of the limb affected has been found of value, based as it is upon well-known observations of patients that the opposites of these increase their sufferings. Other measures to be noted are hydrotherapy, electricity (Eulenburg and Schütz found benefit from the use of the constant current), massage (although Barlow says it is of doubtful value and unbearable during the paroxysms). Of course antisiphilitic remedies are indicated in cases in which that disease is believed to underlie or complicate erythromelalgia, and among drugs which are more or less approved are arsenic, antipyrin, the bromide of potassium, morphine (Morgan reporting a case of recovery after hypodermic injections of morphine and atropine twice a day for three weeks), the salicylates, atropine, and ergot internally as well as ichthyol externally. It should also be remembered that spontaneous recovery has taken place in some cases. Further than this, the several cases referred to above are evidence that surgical measures, such as the stretching of nerves, their resection, and the amputation of toes and fingers, have brought relief in certain instances. It should be noted, however, that gangrene followed operative procedures upon nerve and vein in one case of Weir Mitchell's and upon amputation of a toe in another.

The references given below are mainly to the chief articles of the last three years, the reader being referred to the essays of Lewin and Benda and of Kahane for full bibliographies.

J. Haven Emerson.

## REFERENCES.

- Allchin, W. H.: A Manual of Medicine, vol. iii., p. 382, London, 1901.  
Auerbach, S.: Ueber Erythromelalgie, eine klinisch. u. anatom. Untersuchung. Deutsche Zeitschr. f. Nervenheilk., Leipzig, 1897, xi.  
Barlow T.: Allbutt's System of Medicine, vol. vii., p. 607, 1899.  
Cassirer, R.: Die vasomotorisch-trophischen Neurosen, Berlin, 1901.  
Collier, J.: The Occurrence of Erythromelalgia in Diseases of the Spinal Cord, an account of ten cases. Lancet, 1898, ii., 401.  
Elsner, H. L.: Recent Experiences with Erythromelalgia. Medical News, New York, 1901, lxxviii., p. 405.  
Eulenburg, A., in Realencyclopædie der gesammten Heilk., 3te Aufl., 1895, vol. vii.  
Kahane, M.: Erythromelalgie. Centralbl. f. d. Grenzgebiete d. Med. u. Chir., Jena, 1900, vol. iii., with extensive bibliography.  
Lévi, L.: De l'Erythromelalgie, Syndrome de Weir Mitchell. Presse méd., Paris, 1897, ii., 157.  
Lewin u. Benda: Erythromelalgie. Berlin. klin. Woch., 1894, full bibliography to date.  
Mitchell, Weir: Phila. Med. Times, vol. iii., 1872-73. Amer. Journ. Med. Sci., July, 1878.  
Mitchell, Weir, and Spiller, W. G.: A Case of Erythromelalgia with Microscopical Examination of an Amputated Toe. Amer. Journ. Med. Sci., 1899, i.  
Reynolds, H. B.: Erythromelalgia with Report of a Case. Occident. Medical Times, San Fran., 1903, xvii.  
Sachs, B.: Erythromelalgia. Journ. Nerv. and Ment. Dis., New York, 1899, xxvi., 372.  
Sachs, B., and Wiener, A.: Die Erythromelalgie, eine klinisch-anatomisch. Besprechung. Deutsche Zeitschr. f. Nervenheilk., Leipzig, 1899, xv.  
Saville, T. D.: On Various Angioneurotic Disturbances, including Erythromelalgia. Lancet, 1901, i.  
Schütz, R.: Erythromelalgie u. Hautatrophie. Dermat. Zeitschr., Berlin, 1899, vi.  
Shaw, H. B.: The Morbid Anatomy of Erythromelalgia, Based upon the Amputated Extremities of Three Cases. Brit. Med. Journ., 1903, i.

Starr, M. Allen: Organic Nervous Diseases, New York and Philadelphia, 1903.  
Taubert: Ueber Erythromelalgie bei Syringomyelie. Deutsch. med. Woch., Berlin, 1903, xxxix.

**EUCAINE** is a name applied to two different but closely allied local anesthetics distinguished as *Alpha-eucaine* or *Eucaine "A"* and *Beta-eucaine* or *Eucaine "B"*.

The anæsthetic effect of cocaine, which is methyl-benzoyl-ecgonine,  $C_{17}H_{21}NO_4$ , was found to depend on the presence of both the methyl and the benzoyl groups and not on the ecgonine radical. So with the desire of obtaining the anæsthetic effect of cocaine without its toxicity, other methyl-benzoyl compounds were designed. Of these Eucaine "A" was submitted to the profession, and was for a time extensively employed; but its very irritating effects have so militated against its desirability that it has been largely replaced by its congener, Eucaine "B," a compound of less toxicity and less irritating properties.

*Alpha-eucaine*,  $CH_3.N.C_2.(CH_3)_2.(CH_3)_2.(CH_2)_2.CC_6H_4.COO.COCH_3$ , is methyl-benzoyl-tetra-methyl-hydroxy-piperidine-carbonic-acid-methyl-ester, a derivative of tri-acetone-amine. Its hydrochloride occurs as a bitter white crystalline powder soluble in 10 parts of cold water, 7 of boiling water, less than 2 of alcohol, and 13 of glycerin, and is very slightly soluble in ether and the fixed oils.

*Beta-eucaine*,  $H.N.C_2.HCH_3.(CH_3)_2.(CH_2)_2.C.C_6H_5.COO.H$ , benzoyl-vinyl-diacetone-alkamine, is also a bitter white crystalline powder, and its hydrochloride dissolves in 23 parts of water, 12 of boiling water, 30 of alcohol, and 35 of glycerin. It is insoluble in ether and almost insoluble in the fixed oils.

Both eucaines have the nature of alkaloids, and their hydrochlorides have been the salts in common use; but the acetate of beta-eucaine is now recommended as it is readily soluble in water. The solutions of eucaine salts are not decomposed by boiling, so may be sterilized.

The pharmacological action of the eucaines has been studied by Cushman, Vinci, Ver Eecke, and others. The salts are not absorbed by the unbroken skin, but, applied to mucous membranes or injected into the tissues, they paralyze the sensory nerves and their terminal endings at the site of application and are powerful local anesthetics. They are said to produce local congestion in mucous membranes.

In large dose they weaken the heart by direct depression of the cardiac muscle and its contained ganglia, and in addition lower blood pressure by dilatation of the arterioles. The respiratory centre is at first stimulated, later paralyzed, so that death takes place from asphyxia (paralysis of respiration). The cerebral centres are stimulated with the production of tonic and clonic convulsions; later they are paralyzed. There is no dilatation of the pupil or disturbance of the accommodation of the eye, but the conjunctiva is congested. The superficial epithelium of the cornea is not affected. The kidney cells are stimulated and the quantity of urine is increased, with increased elimination of nitrogen, phosphorus, and chlorides. The drug is not found in the urine, and apparently undergoes decomposition in the body.

To produce general poisoning in rabbits and guinea-pigs it requires 0.15-0.2 gm. of eucaine "A" per kilo, and 0.4-0.5 gm. of eucaine "B." Cocaine is four times as poisonous as eucaine "B," and only slightly more toxic than eucaine "A."

The uses of beta-eucaine as a local anæsthetic are practically those of cocaine, so we need not here enumerate its therapeutic applications. The consensus of opinion among surgeons (Bier, Bainbridge, Moyer) would seem to indicate that it is weaker as an anæsthetic than cocaine, whether employed subcutaneously or in spinal analgesia. Wallis found that the amount required for a small operation averaged 3 i.-iss. (4-6 c.c.) of a four-per-cent. solution, but G. W. Crile performed a painless duodenotomy with 8 c.c. (5 ij.) of a two-per-cent. solution.

Nearly all writers agree that eucaine tends to increase a hyperemia of the conjunctiva or nasal mucous mem-

brane, and Dawbarn and others prefer it for the removal of tonsils, adenoids, and other hypertrophied tissues, as it does not cause a shrinkage like cocaine. Poole prefers cocaine in iritis, as eucaine increases, or at least does not decrease, the anterior congestion.

In our experience eucaine applied to mucous membranes is slower in its action and much weaker than cocaine; used subcutaneously it is somewhat weaker. We had several cases of local gangrene following its hypodermic use in abdominal and pleural tapping, though in each of these instances the injection had been preceded by the ethyl-chloride spray. Cocaine under similar conditions never produced a slough. Da Costa noted a slow, persistent sloughing, especially in fatty tissue, bursa, or tendon sheaths. He also noticed inflammation following its use in the bladder. Shastid reports the occurrence of amblyopia, rapid pulse, and delirium following the application of a five-per-cent. solution to the inferior turbinate.

Beta-eucaine is, then, a drug of anæsthetic action resembling that of cocaine, but somewhat weaker. It produces hyperemia rather than the ischaemia of cocaine, and has no effect on the pupil, accommodation, or the corneal epithelium. In the ordinary dosage it is non-toxic, and is reported to be well borne where there is an idiosyncrasy against cocaine. Lilienthal has frequently used four to ten grains without unpleasant consequences. No eucaine habit is known. The drug keeps indefinitely and can be sterilized by boiling.

Solutions of one- to four-per-cent. strength in normal salt are commonly employed, but stronger solutions, obtained by heating the liquid and using warm, are sometimes preferred. Von Mikulicz uses the following:  $\beta$  Cocainæ hydrochloridi, 0.5 gm. (gr. viiss.); beta-eucainæ hydrochloridi, 0.5 gm. (gr. viiss.); sodii chloridi, 2 gm. (gr. xxx.); aquæ, q.s. ad 1,000 c.c. ( $\mathfrak{z}$  xxxii).

W. A. Bastedo.

**EXOPHTHALMIC GOITRE.**—(Synonyms: Graves' disease; Basedow's disease.) These names have been indifferently used during the last sixty or more years to express a fairly well-defined disease in which more or less enlargement of the thyroid, protrusion of the eyes, and certain nervous disturbances (including tachycardia) form the prominent symptoms. The Irish physician, Graves, who described the coexistence of palpitation of the heart with enlargement of the thyroid as an affection more or less related to hysteria, was antedated in his observations by Parry, who mentioned the same combination together with exophthalmos in 1825. Some years later Basedow also observed the existence of exophthalmos in similar cases, and gave the description which has connected his name with the disease. Charcot, too, in 1844 and 1845 described such cases at the Salpêtrière. Since their time an enormous literature has appeared in which, while the objective descriptions remain very constant, the most divergent theories have been advanced to account for the symptoms. These we may detail in discussing the etiology of the disease.

Exophthalmic goitre is an affection which occurs most frequently in women, although cases are by no means rare in which the same phenomena are seen in men. No very precise age limits can be set, but the majority of the cases appear to begin after the age of puberty, and to increase in number as the climacterium is approached, the onset being most frequent, according to Osler, between the ages of twenty and thirty. No particular station in life seems to predispose to the disease, but it is usually observed that the individuals belong to neuropathic families in which cases of epilepsy, hysteria, chorea, or even some form of insanity have occurred. Combinations of epilepsy and exophthalmic goitre in the same person have been described, in which cases the epileptic seizures usually give place to the symptoms of the other disease. Exophthalmic goitre is a very widespread disease, not at all localized in certain areas, as is the case with other forms of goitre and with endemic myxœdema or cretinism. Indeed, although cases in which exophthalmic