

PART III.

SPECIAL REPORTS.

REPORT ON MATERIA MEDICA AND THERAPEUTICS.*

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Salicylic Acid.—It has long been known that the salicylic acid prepared by Kolbe's reaction from commercial phenol (carbolic acid) contains a variable quantity of impurity or impurities. Among these impurities there are sometimes found a red colouring matter, unaltered phenol, and apparently other substances, which had been associated with phenol in the crude carbolic acid. These substances it has been proposed to remove by dialysing the acid, on the assumption that, unlike salicylic acid, they are uncrystalline, and therefore incapable of dialysis. Therapeutic observation has, however, disclosed the fact that both the commercial salicylic acid and that purified by dialysis produce effects, when administered to the human subject, which are not observed to result from the administration of the pure salicylic acid prepared from the methyl salicylate contained in the natural oil of wintergreen. Many years ago the late Mr. John Williams demonstrated experimentally that the artificial salicylic acid, as met with in commerce, contained an admixture to the extent of some fifteen per cent. of another acid which he considered was probably derived from cresylic acid. The subsequent observations of Professor Latham—that artificial salicylic acid had a different effect when administered medicinally from that of the natural acid—increased the

* The author of this Report, desirous that no contribution to the subjects of *Materia Medica* and *Therapeutics* should remain unnoticed, will be glad to receive any publications which treat of them. If sent to the correspondents of the *Journal* they will be forwarded.

This Report is based upon an article by the writer in the "Year-Book of Treatment" for 1891.

doubt as to the fitness of the artificial acid for medicinal purposes, but beyond that no great attention was paid to the matter. At a still later period Professor Charteris ascertained, from direct experiments with the artificial and natural salicylic acids, that there was a distinctly different physiological effect when one or other of them was administered, and that while the natural acid produced no bad effects, the artificial acid was decidedly toxic. It therefore became important to examine more closely the characteristics of the adventitious substance or substances associated with the salicylic acid obtained synthetically from carbolic acid, and to seek for some efficient means of purification by which the objectionable admixture might be eliminated.

It is to this latter problem that Professor Dunstan has directed his attention, and he has succeeded in defining the nature of the above-mentioned impurity, separated from artificial salicylic acid by Mr. John Williams, as well as that of another impurity subsequently obtained and sent to him by Mr. Williams. Professor Dunstan has also found a third impurity in the course of his investigation, and these have been submitted to physiological tests by Professor Charteris, with the result of showing that two of them produce poisonous effects when administered to animals. The experiments instituted for the purpose of separating these impurities from artificial salicylic acid have shown that the method adopted by Mr. John Williams of fractional crystallisation of the calcium salts is not well adapted for attaining that object, and after many unsuccessful attempts Professor Dunstan has devised a method of purification which appears to be capable of separating the true salicylic acid from the other acids which are associated with it in the artificial product met with commercially.—(*Pharm. Journ.*, Nov. 15, 22, 1890.)

Chloroform, Action of.—It would not be possible to give in a few words an abstract of recent work upon this most important subject. Suffice it to point out that the first portion of the "Report of the Hyderabad Commission" (*Lancet*, January 18, 1890) deals with the much-disputed question—"Is it possible by the inhalation of chloroform to cause sudden stoppage of the heart before the respiration is affected?" The result of the investigations carried out upon several hundred animals, dogs and monkeys, was, that in every case where chloroform was pushed, the respiration failed at a time of from one to ten minutes before the heart ceased beating, or, in other words, that chloroform always kills by asphyxia.

But Professor M'William's report, presented to the Scientific Grants Committee of the British Medical Association (*Brit. Med. Journ.*, 1890) is in sharp conflict with this view. He appears to demonstrate, in a very unequivocal way, that chloroform exerts a direct influence upon the heart—depressing its energy, diminishing its tone, and dilating its chambers. Moreover, such a depressing effect may be brought about by chloroform when given mixed with abundance of air (under 4 per cent. of chloroform vapour), and when the amount of the anæsthetic administered is not sufficient to abolish the conjunctival reflex. The mode of cardiac failure under chloroform is not a sudden arrest of the rhythmic action, but a more or less sudden dilatation and enfeeblement of the organ, causing the rhythmic contraction to be ineffective. Examples are given of cardiac failure, while the respiration went on for many minutes.

Mr. Alexander Wilson, of Manchester, contributes some excellent critical notes upon the "Report of the Hyderabad Commission." His observations throw light upon the apparent contradictions between the results obtained by experiments on animals and those obtained by clinical experience on human subjects. He points out that the extensive experiments of the Commission have left the chloroform question in the following condition:—It was not found possible to directly paralyse or affect the heart by chloroform in some 600 administrations. Death from chloroform is due apparently to paralysis of the vaso-motor and respiratory centres; probably one or both of these may be affected. This paralysis may set in very suddenly, with hardly any warning; it is as far beyond treatment as cardiac paralysis, and it is as fatal. It cannot be too strongly insisted that the work of the Commission gives us no greater confidence in chloroform than we had before. Its physical and chemical properties remaining the same, the danger of permitting the patient to inhale an overdose will remain as great as ever.—(*Med. Chronicle*, Feb. and April, 1890).

Professor Wood, in his able address (*Brit. Med. Journ.*, Aug. 16, 1890), also traverses the results of the Hyderabad Commission. He claims that the fact is well established, both by experiments upon animals and by reliable observations upon man, that chloroform is capable of causing death either by primarily arresting the respiration or by primarily stopping the heart, but that commonly both respiration and cardiac functions are abolished at or about the same time.

Professor Wood sums up in a few words the rules for the proper treatment of accidents during anæsthesia.

Avoid the use of all drugs except strychnin, digitalis, and ammonia.

Give the tincture of digitalis hypodermically.

Draw out the tongue, and raise up the angle of the jaw, and see that the respiration is not mechanically impeded.

Invert the patient briefly and temporarily.

Use forced artificial respiration promptly, and, above all, remember that some at least, and probably many, of the deaths which have been set down as due to chloroform and ether have been produced by the alcohol which has been given for the relief of the patient.

Recent Hypnotics and Analgesics.—This important class of drugs is engaging the attention of pharmacologists and therapeutists both at home and abroad, and the Therapeutic Committee of the British Medical Association have taken hypnotics as the subject of investigation for the current year. Dr. Leech, of Manchester, introduced for discussion the subject of hypnotics at the Leeds meeting of the Association in 1889. His excellent paper (*Brit. Med. Jour.*, Nov. 2, 1889) sets forth so clearly and succinctly what is known of hypnotics, and what is required to be known, that it deserves to be studied, and a few of his observations may be fitly reproduced here. His communication dealt chiefly with urethane, methylal, amylene hydrate, sulphonal and paraldehyde—*i.e.*, hypnotics connected with the fatty series. In regard to hypnotic power, the order of potency seems as follows:—(1) sulphonal; (2) amylene hydrate; (3) paraldehyde; (4) urethane; (5) methylal. None of these drugs equals chloral hydrate in the certainty of its effects. Comparing the doses quantitatively, it appears probable that a dose of sulphonal has, as a rule, about the same soporific action as three-fourths its weight of chloral; and von Mering is of opinion that half a drachm of amylene has the same power as 15 grains of chloral or 45 minims of paraldehyde. The effects of sulphonal are sometimes very enduring, and Dr. Leech has known a patient sleep twenty hours after 20 grains, and troublesome nervous effects may last many days after a single dose.

It is with regard to the influence on circulation and respiration that the newer hypnotics differ so markedly from the older. The newer drugs are to a large extent devoid of the evil influence which chloral, for example, is liable to exert upon the heart and

respiration. They very rarely affect the circulation and respiration unless given in doses such as are not used medicinally.

Dr. Leech finds that urethane, in doses of 20 to 30 grains, is often very successful in slight cases of insomnia, and of all the hypnotics it is the least likely to give rise to dizziness, headache, or other discomfort.

With regard to the use of hypnotics in mental disease, Dr. Leech inclines to paraldehyde as the best for continuous use, and Dr. Clouston likewise regards it as the purest and least harmful hypnotic when insomnia is marked and intractable.

Urethane.—Dr. Gordon, of Aberdeen, has made a valuable experimental contribution to the pharmacology of urethane—a drug which has not lately been in much demand. He has also examined its actions as a hypnotic on subjects in good health and in disease when sleeplessness was a factor. As the result of the administration in a considerable number of cases of insomnia it had a distinct hypnotic action when given in doses of 30 to 60 grains. The sleep which it produced was always pleasant. The patient awoke without any confused feeling, never complained of headache, loss of appetite, or any disagreeable sensation, but, on the contrary, expressed gratitude for the refreshing sleep. It was noticed, however, that in many of the cases a rapid tolerance of the drug took place. It was repeatedly found that, although a dose of 30, 45, or 60 grains, when administered for the first or second time, produced some hours of tranquil sleep, when the same dose was given on the succeeding night it was found that no hypnotic action followed.

Several friends who tested the action of the drug in the insomnia of cerebral cases in asylum practice, found that in large doses—namely, 60 to 100 grains, it was unreliable; in many cases its hypnotic action was not noticeable after the first few doses. No period of excitation was observed to follow the administration of any dose, and, when the drug acted, the onset of sleep was within ten to fifteen minutes.

In point of reliability, urethane compares unfavourably with paraldehyde, which has no specially marked period of toleration, and which, in many cases, can be taken for months with equally reliable results. This unreliability of urethane seems to have been noticed by various observers, among others Otto and König.

No hypnotic effect was produced upon healthy subjects by administration of large doses, 40 to 60 grains, in the morning. In

large and continued doses it is liable to cause anorexia, and even to induce vomiting.—(*Brit. Med. Journ.*, Nov. 2, 1889).

Of the compounds *somnal* and *phenylurethan*, introduced respectively by Radlauer and Giacomini, not enough is known to speak with certainty as to their value.

Aristol.—Some time ago iodol was introduced as a pleasanter substitute for the malodorous iodoform, and now a new competitor appears under the name of aristol. It is dithymol-diiodide, and is prepared by adding a solution of iodine in iodide of potassium to an alkaline solution of thymol. It contains 45·8 per cent. of iodine. It is a red-brown powder, odourless, unirritating, insoluble in water and glycerin, slightly soluble in alcohol, and freely so in ether and fixed oils. It is decomposed by warmth and by exposure to light.

Eichhoff first tested it therapeutically, and reported very favourably of its action in various skin diseases—viz., eczema, ringworm, ulcers, and lupus. He used a 3 to 10 per cent. ointment made with vaseline.—(*Monatsh. für prakt. Dermat.*, 1890.) In a subsequent paper he records his further experience of the drug, and concludes that it is perfectly harmless, and is of great service in psoriasis, eczema, ringworm, and ulcerating syphilis and lupus.—(*Med. Chron.*, Aug., 1890, from *Deutsche med. Wochens.*, 1890.)

Although it has been before the profession such a short time, an extensive series of publications upon its use has appeared, and in the main they confirm and add to the favourable results recorded by Eichhoff. An abstract of recent papers is to be found in *Med. Chron.*, July, 1890.

In France, Drs. Brocq and Gaudin found it to favour cicatrization in a most striking manner. In chronic rhinitis and eczema it has proved of much service in the hands of Drs. Hughes and Lowenstein; and in gynæcological practice Dr. v. Swieicki, of Posen, reports very favourably of it. Likewise from Spain come good reports, from Drs. Buscalla, Bufill, and Estapé.—(*Therap. Monatsh.*, Sept., 1890.)

Creolin.—This antiseptic and disinfectant seems to be holding its place, and is well spoken of by Dr. Otis (*Boston Med. and Surg. Journ.*) and Dr. Lebowicz (*Revue Gén. de Clin. et de Thérap.*, 1889.)

But it should be remembered that it has given occasion to several cases of poisoning. Three cases are detailed by Dr. Dinter (*Therap. Monatsh.*, Dec., 1889). In a case under Dr. Ackeren, a man swallowed nearly 9 oz. of creolin, and became unconscious,

but ultimately recovered (*Brit. Med. Journ.*, Jan. 11, 1890, from *Berlin. klin. Woch.*).

Dr. Zielewicz, of Posen, has formed a high opinion of the merits of creolin, and has used it for the last two years in his private and hospital practice.

According to Henle's analysis, creolin consists of four groups of compounds, viz.—(1) soaps, (2) creolin oil, (3) phenols, (4) pyridines (*Therap. Monatsh.*, April, 1890).

Dr. Schwinz has obtained satisfactory results from creolin in the treatment of diseases of children (*Brit. Med. Journ.*, Nov. 7, 1889).

Ichthyol.—Professor Gadde thinks that ichthyol is entitled to a foremost place among recent drugs, and his observations are quite in accord with those already published by Unna. He especially recommends it in anomalies of the circulation with dilatation of the blood-vessels.—(*Therap. Monatsh.*, 1890.)

Dr. Freund, of Strassburg, has a high opinion of its value in the treatment of inflammatory affections of the female sexual organs.—(*Berl. klin. Woch.*, 1890.)

Diuretin.—Under this name a sodio-salicylic compound of theobromine, corresponding to one of the so-called soluble salts of caffeine, has been introduced as an advantageous diuretic (*Apoth.-Zeit.*, Dec. 14, p. 1338). According to Dr. Gram, of Copenhagen, theobromine is a diuretic, acting directly upon the kidneys, differing from caffeine in not affecting the central nervous system, and therefore not causing sleeplessness and restlessness. It is said to have produced satisfactory diuresis in cases of renal and heart disease in which digitalis and strophanthus have been without effect. But as the free alkaloid requires about 1600 parts of water for its solution it is not readily absorbed, and gives rise to disturbance of the stomach. Diuretin, on the other hand, is alleged to produce the beneficial effects of theobromine without the unpleasant symptoms. It is described as occurring as a white powder containing 48 per cent. of theobromine, dissolving with the aid of heat in less than half its weight of water, and remaining in solution after the liquid has cooled. It is administered to the extent of about 6 grammes daily in 1 gramme doses.—(*Pharm. Journ.*, Dec. 28, 1889.)

Orexin (ὄρεξις, appetite).—Penzoldt believes that in this substance the true stomachic has been found, one which has the power of exciting the appetite, aiding digestion, and stimulating absorption of the products of digestion.

The hydrochlorate of orexin (or phenyldihydroquinazoline) occurs under the form of colourless or nearly colourless needles. Orexin is almost insoluble in water, but the hydrochlorate is readily soluble in warm water. It is sharply irritant to the nasal mucous membrane, has a bitter taste, and leaves a tolerably strong burning sensation upon the tongue.

The author employs the following formula:—

Hydrochlorate of orexin	-	-	-	2 grammes.
Extract of gentian	-	-	-	q. s.
Powdered marsh-mallow	-	-	-	q. s.

Made into 20 pills. From 3 to 5 daily. Or it may be given in wafers.

Experiments on thirty-six patients showed that in many cases the drug restored lost appetite. This effect rarely occurred after the first dose; usually it came on after several doses given in the course of a few days. Orexin has a prompt effect in anæmic and cachectic individuals, in patients on whom operations have been performed, in those suffering from phthisis, &c. The drug is of special value in commencing pulmonary tuberculosis, and Dr. Penzoldt in many such cases observed a considerable increase of the weight of the body. No disagreeable after-effects had been observed, except occasional burning along the œsophagus and rare and transitory vomiting (*Therap. Monatsh.*, Feb., 1890). Dr. Martins, of Breslau, has published the results of a large number of experiments made with a view to determine how far the claims recently put forward on behalf of orexin as an appetite-producer have a foundation in fact (*Deutsche med. Woch.*, May 15, p. 427). In twenty cases the pills were administered without informing the patients as to the reason why they were given; in five cases the patients were told that the pills contained something that would improve the appetite, the results being checked by the use of pills containing no orexin, but made up to resemble the orexin pills; in three cases orexin pills and plain pills were administered comparatively without any statement to the patients, and in seven other cases the conditions were varied in different ways. Out of the twenty-nine cases in which orexin was administered the appetite showed some improvement in five, but not to any considerable extent; in the other twenty-four cases the orexin did not seem to exercise any influence upon the appetite; whilst in five cases an improvement in appetite followed the administration of pills although they contained no orexin. Dr. Martins considers there-

fore that the general results of his experiments have not afforded any distinct and indisputable evidence of the action of orexin in the direction of improving the appetite.—(*Pharm. Journ.*, May 31, 1890.)

Chloralamide.^{*}—This hypnotic has attracted a good deal of attention, and the verdict, upon the whole, is in its favour. A good abstract of the literature is given by Dr. Leech.—(*Med. Chron.*, April, June, 1890).

Halasz (*Wiener med. Wochensch.*, 1889, 38, 39) reports that it has no influence upon the circulation, and recommends its employment even when the heart is weak and irregular. In doses of 30 to 45 grains it is a useful but not a certain hypnotic, and seldom produces any serious after effects. Occasionally, headache, giddiness, and nausea follow its administration.

Alt, on the other hand (*Berl. klin. Woch.*, 1889, 36), found the drug ineffective in twelve out of forty-one cases. He noted, also, that doses larger than 45 grains were apt to cause, even in healthy people, dizziness and headache, or a condition like that of intoxication, which, however, does not last long.

The action of chloralamide upon the circulation and respiration has been examined by Langgaard and by v. Mering and Zuntz (*Therap. Monatsh.*, Oct., Dec., 1889, Jan., 1890). The former finds that a distinct decrease in blood-pressure is caused (in rabbits) by the drug, and that it should only be cautiously used in cases of heart disease. But v. Mering and Zuntz dissent from these conclusions, and they point out that since sleep itself depresses the blood-pressure, every hypnotic must to a certain extent lead to this effect. They deny also the lowering effect of chloralamide upon the respiratory centre, observing that the effect of sleep is to decrease the production of carbonic acid, which is the stimulant of the centre. The difference of opinion between these observers is not very serious, and Langgaard allows that in medicinal doses this action of chloralamide will usually be unimportant, but in some pathological conditions might lead to danger. And Robinson (*Deutsche med. Wochensch.*, 49, 1889) has several times observed dangerous symptoms—viz., diminished tension and increased frequency of pulse—after the administration of chloralamide.

^{*} A substance, unfortunately named *chloralimide*, has been lately described by Pinner and Fuchs, and is said to be an active antipyretic and analgesic. It is obtained by heating chloral-ammonia.—*Pharm. Journ.*, March 29, 1890, from *Compt. Rendus*, cix. 817.

Umpfenbach has likewise met with unpleasant symptoms of depression after chloralamide, and, in three cases, erythematous eruptions (*Therap. Monatsch.*, Feb., 1890). It is best ordered an hour or more before going to bed, and may be taken as a powder, washed down with milk, water, or coffee, or in solution with syrup, or it may be dissolved in wine or beer.

In the Richmond Asylum, Dublin, Dr. Cope (*Dublin Journ. Med. Science*, Feb., 1890) has found chloralamide to be a valuable hypnotic for the insane. Its solubility in water is 1 in 14. A dose of 25 to 35 grains was sufficient to cause sleep in patients suffering from melancholia and chronic mania, but in cases of acute mania 40 to 50 grains were required. No recognised ill-effects followed the continued use of this drug for eight days. In one case only was its use followed by giddiness and sickness, with dry, brown tongue. Sphygmographic tracings showed no evidence of lowering of blood-pressure.

Sulphonal.—No remedy of recent date has excited more rapid interest than sulphonal, since the announcement of its hypnotic qualities by Kast, in 1888.^a It has been described as a medicine which produces something nearly resembling a natural sleep, with no bad effects, save that it leaves behind it a somnolent tendency easily renewed. Altogether the reports in its favour outweigh those of the opposite tendency.

Naturally it was welcomed by those who treat insanity, and extensive experience has confirmed its utility in this class of practice. An interesting discussion upon the action of sulphonal took place at the Medico-Physiological Society of Paris (reported by Dr. Ireland in *London Med. Recorder*, Dec. 20, 1889). The majority of the speakers, including Drs. Voisin, Febvre, Garnier, Pachoud, and Claret, while acknowledging occasional ill results, testified to the value of sulphonal in mental cases, and it is noticeable that several of them prescribed the drug in very large doses—viz., 4 and 5 grammes. On the other hand, Dr. Marandon de Montyel has either the merit of seeing the dangers of sulphonal, or has been singularly unfortunate in his trials of the drug. He even goes so far as to say that, in doses of 3 to 4 grammes, sulphonal is not a medicine but a poison. It often failed to induce sleep, and in a large number of cases it evoked alarming symptoms in the intellectual functions, and caused disorders of the motor system and of the digestive tract.

^a See a valuable "Contribution to the Study of Sulphonal," by Dr. J. Gordon.—*Brit. Med. Journ.*, March 29, 1890.

Dr. Knoblauch (*Therap. Monatsh.*, Nov., 1889) substantially agrees with Dr. de Montyel. Neither does Dr. Malshni, of Moscow, think highly of sulphonal in asylum practice, and he does not regard it as a very sure or satisfactory hypnotic (*London Med. Recorder*, Nov., 1889). Dr. Knaggs reports a fatal case of sulphonal poisoning (*Brit. Med. Journ.*, Oct. 25, 1890). But Dr. Matthes' report of it, from von Ziemssen's clinic, is more encouraging, and the summary of his observations is:—(1) Sulphonal is a useful hypnotic, though not absolutely certain in its effect. (2) It is preferable to other hypnotics on account of its odourlessness and tastelessness, and its negative action on the vital organs. (3) Undesirable secondary symptoms are infrequent and unimportant. (4) The dose must be varied according to individual idiosyncrasies. For most patients 1 gramme suffices to produce a hypnotic effect without secondary symptoms. If the latter occur, the dose must be made smaller. (5) It is advisable to give the drug at least an hour before going to bed, as its effect is slow. (6) If pain of non-neuralgic origin or distressing cough is the cause of agrypnia, sulphonal is useless. But in many neuralgic affections it appears to have a very good effect.—(*London Med. Recorder*, May 20, 1889.)

Dr. Field remarks that, in America, so much prejudice against chloral has been awakened that physicians felt the need for something to supersede it. Sulphonal is, in his opinion, a first-rate hypnotic. Dr. Field's experience of sulphonal extends over fifteen months, during which he prescribed it in 200 cases. As to dose, he considers that 10 grs. are commonly enough, 15 grs. are often too much. A comforting point about sulphonal is that with frequent use the effective dose may be diminished. It may be laid down as a rule that a patient who does not sleep with 20 grs. will not sleep with any dose. Sulphonal is especially indicated for cases of sleeplessness due to worry or brain disturbance of any kind, and for those cases where chloral and opium are contra-indicated.—(*London Med. Recorder*, Jan., 1890.)

Dr. Steiner thinks highly of sulphonal, and relates an interesting case of a patient of his, aged fifty-four, who, within eleven months, took 300 grammes of sulphonal for the relief of sleeplessness. No bad symptoms were at any time noticed, and the patient gained steadily in health and nutrition.—(*Therap. Monatsh.*, Oct., 1889.)

In favour of sulphonal speak also Dr. Franz, of Breslau (*Therap. Monatsh.*, März, 1890), and Dr. Rackel.

Trional and Tetronal.—A few months since Messrs. Baumann & Kast published (*Zeitsch. f. phys. Chemie*, xiv. 52) the results of a number of experiments made upon dogs with compounds allied to sulphonal, from which they drew the conclusions that the hypnotic action of this class is a function of the ethyl groups in the compound, and proportionate in the intensity to their number, and that the SO_2 group exercises no influence in this direction. Messrs. Barth and Rumpel have attempted to ascertain how far this statement is confirmed by the effects produced upon human patients by the administration of trional and tetronal, containing three and four ethyl groups respectively, as compared with those produced by sulphonal, which contains two (*Deut. med. Woch.*, August 7th, p. 32). In order to make the comparison as close as possible, the experiments with trional and tetronal were made upon patients that had already taken sulphonal with advantage. The results obtained corresponded to the experience obtained upon dogs only so far as to show that both trional and tetronal possess pronounced hypnotic properties when administered to human beings; but they did not confirm the theory as to their quantitative action, as practically the same doses of the new compounds as of sulphonal were found to be required to produce a certain effect, instead of one-half or two-thirds as expected. At present, Messrs. Barth and Rumpel content themselves with saying that probably the indications for the use of trional and tetronal correspond with those for the use of sulphonal, but that in certain nervous conditions which are refractory towards sulphonal the other compounds might prove more effective. As a hypnotic, tetronal was in fourteen cases superior to sulphonal, in six cases equal, and in four cases inferior. Trional in seventeen cases was superior, in six cases equal, and in seven inferior. No injurious bye-effects were observed in any of the 220 cases in which trional and tetronal were administered.—(*Pharm. Journ.*, August 30th, 1890).

Euphorine.—Dr. Sansoni (*Therap. Monatsh.*, September, 1890) has made a number of observations on the action of euphorine in disease. Professor Giacoso has given the name of euphorine to phenyl-urethan.



a new substance derived from aniline. It is a white, crystalline powder, with faint aromatic odour and slight taste, almost insoluble in water, but quite soluble in weak alcohol. Sansoni first tested

the antipyretic effect of euphorine. In fever, due to a large number of causes, the temperature fell quickly within an hour; the fall reached its maximum usually in three hours, and lasted for five to seven hours, but sometimes not so long, and at other times longer. The subsequent rise of temperature was usually sudden and accompanied by rigours. Its antipyretic action is often greater in certain individuals than in others, and hence it is advisable to begin with small doses. Doses of 15 to 20 grains in twenty-four hours can generally be taken without bad results. It is best to begin with a dose of 3 grains. In rheumatism 15 to 30 grains daily caused disappearance of the pain, swelling, and fever. In chronic cases the good results were slight. In a few cases euphorine acted well as an analgesic, but on the whole the success must be considered small. In chronic ulcers and in ophthalmia the powder proved itself a better antiseptic than any other which the author had tried. On the whole, as an antipyretic, anti-rheumatic, and analgesic, euphorine seems to be inferior to many older remedies of the same nature, and unless future experience bears out the high character given to it by Sansoni as an antipyretic, there is little likelihood of its ever becoming a useful drug.—(Suppl. *Brit. Med. Journ.*, October 18th, 1890.)

Hypnal.—The incompatibility of antipyrin with chloral hydrate is well known, and by the combination of the two is formed a compound not possessing the properties of either of its constituents. Recently Herr Reuter showed that by heating antipyrin with chloral hydrate a crystalline compound could be obtained, which he described as trichloraldehydphenyldimethylpyrazol, and alleged to be without therapeutic value. According, however, to the experience of Dr. Bardet, recently communicated to the Société de Thérapeutique (*Nouv. Rem.*, March 24th, p. 135), this crystalline compound, which he proposes to call “hypnal,” partakes in a marked degree of the properties of both its constituents. Administered in twenty-two cases in doses of one grain (two grains being rarely required) he found hypnal to induce sleep as readily as chloral hydrate, whilst in those instances where the insomnia was caused by pain it seemed to have the same anodyne effect as antipyrin. In addition, spasmodic symptoms, especially cough, appeared to be much abated under its influence. Dr. Bardet states that hypnal consists of about 45 per cent. of chloral and 55 per cent. of antipyrin. It has been found by M. Bonnet that if concentrated solutions of the two constituents be shaken together a

considerable deposit of crystals is formed without passing through the oily stage, and this deposit, by recrystallisation from water, can be obtained in enormous rhombic crystals. If the chloral used be in excess, the crystals take the form of prismatic needles. The compound is said to be free from odour or caustic taste—in fact, according to M. Bonnet, it is tasteless; but Dr. Bardet says that while it is free from the strong taste of chloral hydrate and the bitterness of antipyrin, it has a saline taste, a slight but not disagreeable sensation of chloral becoming perceptible on the tongue after some time. Hypnal is said to dissolve in six to eight times its weight of warm water and melt at 58° to 60° ; it is therefore much less soluble than chloral hydrate or antipyrin.—(*Pharm. Journ.*, May 3rd.)

Exalgin.—This drug belongs to the same group therapeutically as antipyrin, antifebrin, and phenacetin as an analgesic. It is unsuitable as an antipyretic, because, in full doses, it is apt to produce untoward symptoms. The favourable reports of MM. Dujardin-Beaumetz and Bardet regarding its pain-relieving virtues have been confirmed by others, in England and abroad. Professor Fraser, of Edinburgh, speaks highly of it. Of 88 separate administrations of exalgin, in 67 of them pain was relieved. In the groups of “facial neuralgia” and “cardiac angina,” 48 out of 52 administrations were successful. Dose, $\frac{1}{2}$ grain to 4 grains in solution in rectified spirit.—(*Brit. Med. Journ.*, February 15th, 1890.)

Dr. Atkinson regards exalgin as valueless (*Brit. Med. Journ.*, June 14th, 1890), but *contra*, Drs. Herschell and Farrar produce satisfactory evidence of its value in relieving and curing cases of severe and obstinate pains (*Brit. Med. Journ.*, July 19th, 1890). Also, Drs. J. S. Holden, H. G. Molony, and A. H. Walker.

Heinz (*Berl. klin. Woch.*, No. 11, 1890) found it efficacious, in 4 to 7 grain doses, in relieving various forms of pain. Rabow (*Therap. Monatsch.*, Mai, 1890) extols it in migraine and all forms of headache. He reckons that about $3\frac{1}{2}$ grains of exalgin are equivalent to 15 grains of antipyrin. An obstinate case of trigeminal neuralgia, in which phenacetin had been repeatedly given without effect, yielded to the second dose of $3\frac{1}{2}$ grains of exalgin. In severe aural pain, and in trimetus, he considers 3 to 4 grains of exalgin to act as quickly and surely as a subcutaneous injection of morphine. The drug was less successful in sciatica and muscular rheumatism. In no case did any seriously unpleasant symptom follow its use; sometimes transitory dizziness and noises in the ear.

However, Drs. Bokenham and Jones (*Brit. Med. Journ.* Feb. 8th, 1890) record a case in which alarming prostration and cyanosis occurred in a young woman after doses of 2 to 6 grains three times a day, continued for a fortnight. Amongst the bye-effects which have attended it as an analgesic are the following:—Sweating, but this is not common with careful dosing (3 to 6 grains). More frequent is giddiness, which appears in a number of cases in from a quarter to half an hour from the administration; this symptom may amount to a sense of drunkenness, with swimming in the head and noises in the ears. In Bokenham and Jones's case there were darkening of vision, and later, delirium and loss of consciousness. Convulsions occurred in Hepp's case of phthisis in which 4·5 + 7·5 grains were administered. Disturbances of digestion, epigastric discomfort, nausea and vomiting, are rare. Blood changes have not been witnessed in man, but in animals there has been diminution of oxyhæmoglobin. Of rashes there have been observed only erythemata. Prevost counsels great caution in using this aniline derivative, which, as such, may easily damage the blood. He, as well as Heinz, Dujardin-Beaumetz, and Bardet, considers fever to be a contra-indication.—(*Brit. Med. Journ.*, Suppl., Oct. 11th, 1890.)

A curious instance of dangerous and distressing symptoms from 3 grains of exalgin is reported by Dr. G. A. Johnston.—(*Brit. Med. Journ.*, May 3rd, 1890.)

Antifebrin.—Messrs. Bokenham and Jones (*Brit. Med. Journ.*, Feb. 8th, 1890) observed alarming effects, similar to those noted above from exalgin, in a lady, aged forty-three, after 7 grains of antifebrin. An analogous case is reported by Dr. Haley (*Lond. Med. Rec.*, Dec. 20th, 1889; from the *Weekly Med. Review*). But that recovery is possible even after excessive doses is illustrated by two recent cases in Germany. A student swallowed 29 grammes, and a woman 30 grammes. Both were intensely cyanosed, but recovered.—(*Pharm. Journ.*, June 21st, 1890; from *Apoth. Zeitung*.)

An interesting summary of the experience of Russian physicians on the clinical uses of antifebrin will be found in *Lond. Med. Rec.*, July 20th, 1889.

Antipyrin.—Dr. Schwabe reports a case where violent toxic symptoms were observed in a young woman who had been ordered antipyrin in 1 gramme doses for severe neuralgic pains (*Apoth. Zeitung*, June 14th, p. 322). Three minutes subsequently to taking a dose at noon, after a meal, she complained of peculiar oppressive

pain in the back of the head. This was followed quickly by ringing in the ears, giddiness, and a feeling of anxiety; then by tumultuous heart-beat, difficulty of breathing, cold sweat, a strong feeling of heat on the right side of the body and of cold and numbness on the left. In twenty minutes the sight was affected, followed by complete amaurosis, lasting half an hour, when it gradually disappeared. The heart disturbance was excessive, the beats numbering two hundred to the minute during the first hour; the speech also was affected. The symptoms perceptibly decreased during the afternoon and evening, but the patient felt very ill during the next two days, though she eventually recovered without any permanent injury.—(*Pharm. Journ.*, June 28th.)

Phenacetin.—Dr. Collischonn is of opinion that the reason why phenacetin has not won its way as an anti-rheumatic is because it has been given in too small doses. With larger doses Dr. Collischonn has had most satisfactory results in the treatment of rheumatism, and he has given up the use of salicylic acid on account of its frequent unpleasant after-effects. The author cured himself of a rebellious attack of rheumatism in two days by two doses of 2 grammes of phenacetin, while he had previously taken 120 grammes ($3\frac{1}{2}$ oz.) of salol in the course of three weeks without any effect. He recommends at least a trial of phenacetin in all cases of rheumatism, best administered in four doses of 1 gramme (15 grains), or two doses of 2 grains.—(*Therap. Monatsch.*, März, 1890.)

Several observers—viz., Drs. Katz, Sleimann, and Irwin, strongly recommend phenacetin in whooping cough. It may be prescribed dissolved in glycerin, in doses from $\frac{1}{2}$ to 10 grains.—(*Med. Chronicle*, April, 1890; from *Apoth. Zeitung*.)

CANCER OF THE BLADDER.

As a wash for cancerous bladders, M. Ludwig Frey recommends iodoform, 25 grammes; glycerin, 20 grammes; water, 5 grammes; gum tragacanth 12 cgr. Mix. One teaspoonful of this mixture to be added to a pint of tepid water. Three injections to be given daily.

WINE FOR PULMONARY TUBERCULOSIS.

M. V. GIEBERT (*L'Union Médicale*):—E. creasote, 2 to 3 grammes; arsenite of sodium, 0 gr. 04 centigr.; Malaga wine, 500 grammes. Mix. Two small glasses of the wine daily during meals.