PART III.

HALF-YEARLY REPORTS.

REPORT ON

MATERIA MEDICA AND THERAPEUTICS.*

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Art. 4. Amylene hydrate.
   ,, 1. Antifebrin.
   ,, 2. Antipyrin.
   ,, 3. Phenacetin.
   ,, 5. Sulphonol.
   ,, 7. Methylal.
   ,, 8. Cardiac Tonics.

1. Antifebrin (Acetanilide).—An excellent summary of recent literature in reference to antifebrin is given in the Medical Chronicle, July, 1888, and to it we are indebted for the following:—

Since Cahn and Hepp published the first account of this drug in 1886, more than 100 papers have appeared in various languages concerning it, and many additional facts have been recorded with regard to its physiological action and uses. In using antifebrin it is important to remember that it is not readily soluble in cold water—requiring 189 times its own weight for solution—but it dissolves easily in pure ether and alcohol, and is fairly soluble in liquids containing alcohol, as wine. The drug can be readily administered in the form of powder, or in cachets. There is some diversity of opinion as to the range of dosage, but according to the majority of observers 4 to 7 grains are a suitable dose in febrile

* 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.
cases, which may be repeated two or three times, but, as a rule, 30 grains a day is a sufficient quantity; much, however, depends upon the ailment. Phthisical, weakly, and anæmic patients, seem easily affected by antifebrin, and to require small doses. Large quantities are apt to cause cyanosis, cardiac weakness, and collapse.

In typhoid fever, 4 grains every six or eight hours are often sufficient. In rheumatic fever and pneumonia larger doses are usually required. For the relief of pain in neuralgia, &c., from 8 to 15 grains may be given for a dose, and even in doses of 2 grains it efficiently reduces temperature. Children seem to bear antifebrin well, and Widowicz, who has had extensive experience of its employment in the febrile diseases of children, says 1½ grains may be given to those aged three or four years, while doses of 3 or 4½, or even 7½ grains, may be administered to older children. It is worthy of remark that antifebrin scarcely ever causes a cutaneous rash like other antipyretics. Sometimes the profuse sweating is accompanied by sudamina and redness of the skin. Although comparatively insoluble, antifebrin is readily absorbed, for its effects on temperature are usually noticeable within an hour, and sometimes appear in a quarter of an hour. The duration of the reduction of temperature is usually from three to six hours; but, of course, much depends upon the dose and the ailment. When the temperature rises again, chilliness is sometimes noted, but rarely rigors. Almost all observers agree that shivering is less common after antifebrin than after kairin, thallin, and antipyrin. The exact cause of the temperature fall has not been satisfactorily determined, but it is probably due both to increased dissipation of heat, and also to diminished heat production.

Although introduced at first only as an antipyretic remedy, antifebrin has since been strongly recommended, especially by French observers, as a sedative to the nervous system—e.g., in locomotor ataxy, sciatica, lumbago, and other nervous ailments.

As a hypnotic it has been highly spoken of by many observers in affections of the nervous system, as well as in febrile conditions. Kell records a case of acute alcoholism, with rapid pulse and high temperature, in which sleep followed two doses of 10 grains, and became profound after a third dose. The patient woke after a five hours' sleep much better.

2. Antipyrin.—This drug maintains its reputation, and continues to be largely used. As an anodyne, M. Germain Sée was the first
to call attention to the very marked influence of antipyrin over pain, whether administered by the mouth or hypodermically. Since he published his series of cases the drug has been employed tentatively in most civilised countries, and the reports are now coming in. With very few exceptions the experiments have been successful. Fränkel, of Berlin, in order to test its anodyne properties, substituted antipyrin for morphin injections in all the cases under his care. In not a single case did he fail to give relief. He employed it in 5-grain doses, repeating the injection in an adjacent spot if necessary. He proved that the local action of 5 grains of antipyrin was about the equivalent of a thirtieth of a grain of morphin. The influence of the drug was manifested in about fifteen seconds, and lasted from six to eight hours. He expresses the conviction that antipyrin may be used with advantage in many cases in which morphin is at present employed. It produces no disagreeable after-results apart from the slight pain of the injection itself.

Hirsch, of Hanover, is not less affirmative after a trial of the drug in seven cases of severe rheumatic and neuralgic pain. In the United States, Dr. Waugh, of Philadelphia, has employed it successfully in a series of cases of neuralgia, muscular rheumatism, sciatica, &c. In the treatment of sciatica the relief was more prompt and at least as marked as could have been obtained from the use of morphin. He used it in doses of from 2 to 5 grains. Dr. Arca, Professor of Medicine at Buenos Ayres, himself a sufferer from chronic rheumatism, was treated by M. Sée by means of a hypodermic injection of 15 grains of antipyrin, together with from 30 to 60 grains by the mouth, daily. The result was marked relief, though the pain returned directly he discontinued the treatment. There seems no reason to doubt that in antipyrin we possess a powerful anodyne for pain of nervous or rheumatic origin. Dispensed in the form of tablets, it is easily dosed, and may be administered either hypodermically or by the mouth. Beyond the smarting which follows the injection, no after-effects of moment are produced, and it has rarely been known to give rise to inconvenient, much less toxic, symptoms (Brit. Med. Jour., Jan. 7, 1888).

Dr. J. Ogilvey renews his recommendation of antipyrin in migraine. He finds that some cases require larger doses than the 8 grains (hourly repeated) which he first advised, and that double that quantity will then be effectual. For such as are unable to leave home or enjoy travel, to go into crowded rooms, or to venture on certain articles of food and drink, or even medicinal
tonics, there is in antipyrin a promise of immunity from the dreaded headache (Brit. Med. Jour., Jan. 14).

Some interesting and practical notes on antipyrin are contributed by Dr. W. T. Brooks to the Brit. Med. Jour., May 19.

Dr. Kingsbury adds his testimony, based upon the results of treating twenty cases of migraine. Several of the patients having suffered for over ten years, and finding all drugs useless, had become reconciled to being periodically prostrated for one or two days. In every case he ordered 8 grains of antipyrin, dissolved in water or lemonade, to be repeated each half hour until cured, the patient to remain lying down. Most of the cases were quite cured by two powders, but the most obstinate yielded to three, and in no case did the antipyrin fail. A cup of warm tea sometimes seemed to help, and the only inconvenience due to the treatment was, in a few of the cases, considerable sweating.

Many of the patients can hardly credit that instead of being utterly helpless for twenty-four hours they can now cut short an attack in one hour.

There is another great advantage in using antipyrin, and that is that it prevents as well as cures these attacks. One lady, who cannot remember having fewer attacks than three a month, each lasting about thirty-six hours, has been quite free for eight weeks, and this she attributes solely to the occasional use of an antipyrin powder (Brit. Med. Jour., Dec. 24, 1887).

I can confirm these statements, and consider antipyrin to be a most valuable remedy in neuralgic affections.

M. Chouppe has called attention to the good effects of antipyrin in uterine pains after parturition, or in dysmenorrhoea. He believes that it acts upon the spinal cord, and might be administered with advantage during parturition to women of an irritable temperament. It does not interfere with the oxytocic action of ergot (Brit. Med. Jour., Dec. 17, 1887).

Dr. Laget employed antipyrin with complete success in relieving severe labour-pains, continuing for upwards of two days, and which had resisted opiate enemata. The drug was administered by enema, 2 grammes in 100 grammes of water, repeated in an hour (Brit. Med. Jour., Jan. 28, 1888).

Hence it appears, as pointed out by Dr. Neudörfer, that the name “antipyrin” does not represent the whole value of the drug, and that its anodyne and antiseptic properties are of equal, if not greater, importance. The author has often observed that the
hemicrania of women disappeared for a long time after a single subcutaneous injection of antipyrin. The drug was decidedly preferable to morphin, and was, in many respects, quite equal to cocaín. It prevents putrefaction and kills bacteria, and may be used for surgical purposes in a 5 per cent. solution (Brit. Med. Journ., Jan. 21, 1888).

Unpleasant Effects from Antipyrin.—Prescribers who have made much use of antipyrin as an analgesic, have been for some time aware that it was liable now and then to give rise to symptoms of an extremely disagreeable kind. Dr. Allen Sturge records an interesting example of idiosyncrasy, which deserves to be borne in mind. A member of his family liable to migraine was attacked in the ordinary way a few days ago, and he administered for the first time a dose of 5 grains of antipyrin in powder, with the following curious result:—Five minutes after taking it, the "deadly sickness" which was previously present seemed to give way, and an "expanding sensation" was felt, rising from the stomach upwards. Almost immediately she sneezed violently for about twenty times running without pause. The face and eyes became deeply suffused, tears began to flow, quantities of mucus flowed from the nose, the breathing became hard and laboured, accompanied by a feeling of suffocation; there was complete inability to lie down. A violent cough shortly came on, and large quantities of mucus were expectorated; at the same time there was very profuse sweating.

After these phenomena had lasted for about half an hour, intense itching was felt on the insides of both thighs, and on examination there was found a thick outcrop of urticaria, which soon extended on to the abdomen. There was also a strong coppery taste in the mouth—not continuing, but coming on in violent bouts—and an equally strong smell of the same metallic nature, also intermittent. There was loud singing in the ears, which felt intensely congested. The pulse was quick and very full.

After the symptoms had lasted about three-quarters of an hour from the commencement, they gradually disappeared, some tightness of the chest and running at the nose remaining for four or five hours longer. The sickness accompanying the migraine disappeared completely as soon as the drug had begun to work; the headache also disappeared for a time, but came back slightly about four hours afterwards (Brit. Med. Journ., Feb. 4, 1888).

Two cases comparable to the above were recently mentioned in the New York Medical Record. In one case, related by Dr. C. T.
Barber, of Brooklyn, a man took 15 grains immediately before going to bed. He was no sooner in bed than intense itching, starting from the face and extending over the whole body, began to annoy him; the whole body was soon covered by an erythematous blush, which quickly resolved itself into characteristic urticaria. The face was so markedly swollen that the patient’s features were entirely obliterated. The urgent symptoms quickly disappeared after the administration of an emetic, and after mild purgation the patient was again restored to his usual health. In the other case Dr. Whitehouse, of Santiago, gave $7\frac{1}{2}$ grains to a child; in two minutes there was intense pain in the stomach, followed by general urticaria, and finally by loss of consciousness; one-seventieth of a grain of atropin was administered, and in a few minutes the child was well.

3. Phenacetin is a body analogous in its constitution to antifebrin. Its technical name is para-acetphenetidin, and its formula

$$C_6H_4\{OC_2H_5 \{NH.COCH_3\}.$$

It is a nearly white, inodorous, crystalline powder, and perfectly tasteless. Soluble with difficulty in water, a little more soluble in glycerin, but more freely in alcohol. Insoluble in acids (except glacial acetic acid) or alkaline liquids. It was introduced by Drs. Kast and Hinsberg in 1887, and seems to be a reliable antipyretic. Dr. Kobler (Wien. mediz. Wochensch., 1887) and Dr. Hoppe have reported favourably upon it, and Dr. Osborne Grenfell (Practitioner, May, 1888) shows that it is an efficient antipyretic, and that in cases of pyrexia the action of the drug begins within half an hour after administration. The patient generally perspires freely, and feels drowsy, but comfortable. The drug has been extensively used in the Wandsworth and Clapham Infirmary, not only as an antipyretic, but also as an analgesic in neuralgia, and with good results. The most satisfactory dose for an adult is about 8 grains, and children bear it well. In one case the urine became discoloured, but no untoward effects were observed.

Dr. Leyland Roe also found phenacetin to act admirably as an antipyretic in from 4 to 12 grain doses. It exerts a greater and more prolonged effect upon the temperature than antipyrin, and causes neither rigors, nor vomiting, nor nausea, but rather a sense of well-being—the patient frequently becoming cheerful and desirous of food (Brit. Med. Journ., May 26th, 1888).
Dr. Macnaughton Jones specially recommends phenacetin in the evening pyrexial rise of phthisical cases, and states that it does not produce any collateral unpleasant effects.

4. Amylene Hydrate.—A new hypnotic, which appears to possess certain advantages, has been recently introduced by Professor v. Mering. In its physiological effects it seems to occupy an intermediate position between chloral and paraldehyde. Although sold under the name of amylene hydrate, it is an isomer of amylic alcohol (C₅H₁₂O), and its constitution appears to be that of tertiary amyl alcohol \((\text{CH}_3)_2\text{C.OH}\); i.e., dimethylethyl carbinol. It is a clear, colourless, slightly oily liquid, sp. gr. 0.81; boiling point 102.5° C. It has an odour resembling paraldehyde, with a faint suggestion of camphor: it is warm in the mouth, and has a hot aromatic taste, with a slight pungent after-taste. It is only slightly soluble in water (1 in 8), though freely in alcohol, and may be given with extract of liquorice (v. Mering), or in mixture with red wine and sugar (Scharschmidt).

Von Mering gave the drug to sixty patients in doses varying from 46 to 77 grains; he observed no unpleasant after-effects, no nausea, headache, or digestive disturbance. Scharschmidt found that so large a dose was not necessary, although he corroborates v. Mering's statement that even then there was no appreciable disturbance of the respiration or pulse-rate. In 80 per cent. of the cases sound sleep of from five to seven hours' duration was procured by doses which did not exceed 45 grains, and were in some instances as low as 20 grains; by repeating the dose, or giving a larger one, sleep was, in all the cases where failure was at first noted, subsequently obtained. In 24 of Scharschmidt's cases there was much excitement, and by producing sleep under such conditions as mania, delirium tremens, and epilepsy or hysteria with delirium, amylene hydrate appears to have proved itself superior to urethan (Brit. Med. Journ., Jan. 14, 1888).

Dr. G. Avilles has made a number of experiments with amylene hydrate in the clinic of Professor Riegel at Giessen. The drug was tried in various internal diseases, and, in all cases of disordered circulation, it is preferable to chloral, since the latter considerably diminishes the pressure in the vascular system. As a hypnotic it is less powerful than chloral, and more powerful than paraldehyde. After small doses, sleep lasts from two to three hours; after large
doses (2-0 to 3-2 grammes), from six to eight hours. Respiration was not affected, and there was no change in pulse or blood-pressure, except retardation of pulse. There was no bad taste in the mouth, or disagreeable smell of the breath on awakening, such as occurs after paraldehyde.

It may be administered by enema, e.g.:

\[ \text{Amylene hydrate, } - - - 3\text{ grammes.} \]
\[ \text{Aq. destill. } - - - - \]
\[ \text{Gum. Arab. } \text{"} - - - 25\text{ grammes.} \]


Dr. F. Girtler has also tried the drug in 61 cases of various diseases, and he prefers it to chloral, as it has no injurious effect on the heart. Average dose for adults, 3-5 grammes (52 grains), sometimes smaller doses were sufficient; but at certain times larger doses, such as 6 grammes, had to be resorted to. In a few cases headache and slight oppression were complained of, but there was no vomiting *(Berl. klin. Woch., 6. 1888).*

Dr. Buschau thinks amylene hydrate a useful addition to our stock of hypnotics. He tried it in a number of cases in a lunatic asylum, and his net results were: satisfactory sleep in nearly 80 per cent. of the cases; tolerably good sleep in 12 per cent.; failure to induce sleep in 8 per cent.

Amylene hydrate is expensive at present, nearly 30s. a pound.

Dr. Laves reports that more frequently than any other hypnotic it induces deep and refreshing sleep. Unpleasant consequences (excitement, &c.) were very rarely observed; dangerous results never *(Berl. klin. Woch., 21 Mai, 1888).*

Some other tertiary alcohols, viz, tri-methyl carbinol and dimethyl carbinol, have been investigated by Russian observers, but do not seem as yet to have attracted much attention in this country *(Prov. Med. Journ., Jan. 2, 1888).*

5. *Sulphonal.*—Under this empirical name, suggested by Bayer & Co., is introduced a new hypnotic discovered by Professor Baumann. It is an oxidation product of the union of ethyl-mercaptan with acetone, rejoices in the appalling name of “dicy-thylsulphondimethylmethane,” and its rational formula is \((\text{CH}_3)\text{C}-(\text{C}_2\text{H}_5\text{SO}_2)\). It is a very stable compound, crystallises in large colourless
tables, and is perfectly devoid of taste and smell. It dissolves in 18 or 20 parts of boiling water, in 100 parts of water at the ordinary temperature, and is easily soluble in alcohol or ether. It is not affected by acids or alkalies.

Professor Kast, of Freiburg, has tested it therapeutically, and has nothing but praise for this new addition to the materia medica. Twenty experiments with sulphonal on healthy men showed that doses of three or four grammes were borne by adults without the least discomfort or disagreeable after-effect. Employed medically the drug has been given to 60 patients, and 300 observations of its effects were made (Professor Cramer gave it 200 times in the Marburg Lunatic Asylum). The results, almost without exception, were that the patients sank within from half an hour to two hours into a tranquil and sound sleep, lasting from five to eight hours, and awoke feeling perfectly comfortable. A few felt tired and sleepy next day. The digestion, pulse, and temperature were unaffected, and it is curious that no ataxy of any degree or kind was present, whereas this was the most prominent symptom in dogs after large doses. The ordinary dose for man is two grammes (half a drachm). Sulphonal appeared most efficacious in cases of sleeplessness in nervous subjects, but was given with benefit in all kinds of cases, including even cardiac valvular disease (Brit. Med. Journ., Apr. 21, 1888, from Berl. klin. Woch).

Dr. Rabbas confirms Kast's conclusions, and considers sulphonal in doses of from 2 to 3 grammes to be a better and safer hypnotic than amylene hydrate and paraldehyde in larger doses. It does not act so quickly as chloral, but its effects are more enduring. Sleep is induced usually within half an hour. It has no injurious action upon the heart, respiration, appetite, or digestion (Berlin. klin. Woch., April 23rd, 1888.

Drs. Rosin and Oestreicher also conclude that in moderate doses—i.e., 2 grammes, this drug is a non-injurious hypnotic. It is best given in capsules or tabloids (Brit. Med. Journ., May 7, 1888, from Berl. klin. Woch.).

Dr. Lovegrove, on the contrary, found its effects upon patients very discouraging. For several hours after taking the drug no appreciable effect could be observed, but during the greater part of the following day there was extreme drowsiness and considerable cyanosis. The dose given is not mentioned. At present price (May, 1888), 16s. per ounce, it is scarcely likely to supplant its older rivals, morphin and chloral (Brit. Med. Journ., May 26).
6. *Salufer.*—Mr. W. Thomson has discovered that alkaline fluorides are powerful antiseptics, and has proposed as the one best suited for general use the neutral sodium silico-fluoride (*salufer*). It is a white inodorous compound, sparingly soluble in water, about 2½ grains per ounce. Mr. Mayo Robson has used *salufer* extensively in his surgical practice, and is well satisfied with it. A solution of 1 grain to an ounce of water is strong enough for ordinary purposes, and, being unirritating, it is especially suitable for syringing out cavities. He believes that it will prove of great use to obstetricians, and it is a most efficient deodoriser. The solution acts on the glaze of porcelain after long use, and corrodes steel instruments, but sponges are unaffected by it (*Brit. Med. Journ.*, May 19, 1888).

Drs. Hayward and W. J. Sinclair speak highly of it in obstetric and gynaecological practice, and Mr. Penfold of it in dental practice.

7. *Methylal,* a new hypnotic which may possibly render good service in therapeutics. Several observers have studied its action—viz., MM. Personali, Mairet, and Combemale. It is rapidly eliminated, and leaves no ill effects after awakening. It possesses a sweet taste and ethereal odour, and, being soluble in water, is easily administered. In cases of mental disturbance it appears to be worthy of further trial, judging from the results obtained by MM. Mairet and Combemale. The dose is from 3 to 5 grammes and upwards (*Brit. Med. Journ.*, Oct. 22, 1888).

8. *Cardiac Tonics.*—Digitalis still holds its place as the most powerful heart-tonic which we as yet possess, and the most permanent in its effects. But, as we all know, there are good reasons for the zealous efforts made of late years to find some other means of strengthening the heart's action safely as well as certainly in cases of failure of compensation.

Although *strophanthus* has now been on its trial for over two years, it is difficult to decide in exactly what cases of cardiac disease it is preferable to digitalis. Nearly all observers confirm Fraser's original statements without adding any important new facts. However, Guttman maintains that it cannot compare either as a heart-drug or as a diuretic with digitalis. According to observations in Professor Bamberger's clinic, strophanthus was used with success in (1) every kind of disease of the cardiac muscle, in which its effect exceeded that of all other remedies; (2) valvular failures, in which the cardiac muscle could not do the necessary
work, either owing to commencing degeneration or to slight hyper-
trophy; (3) those cases of renal diseases in which the action of the
heart was impaired or normal, but where there was in any case an
increase of the cardiac activity, and thus indirectly increased diuresis. Success was not to be expected in: (1) too advanced
degeneration of the cardiac muscles; (2) valvular failures with
great hypertrophy, where the greatest possible quantity of work
was already done, and an increase of the cardiac energy was no
longer possible; and (3) in renal diseases with cardiac hypertrophy.
Though the indications for the use of strophanthus were in general
exactly the same as those of digitalis, the new remedy had, never-
theless, the advantage that its effect was produced in from ten to
fifteen minutes, and that it had no cumulative effect, and could
thus be given for a long period of time. The tincture recommended
by Fraser (1:20), or the strophanthin itself was used. After the
administration of the first dose nausea and increased action of the
bowels were observed in susceptible persons. Strophanthin could
be given by the mouth without any disagreeable after-effects.
Spartein does not appear to have attracted much attention

PICROTOXIN IN EPILEPSY.

DR. ANNIE NEWS reports a case (New York Medical Journal, July 14,
1888) of the cure of epilepsy by picrotoxin. The patient, aged fourteen,
had been for six months affected with petit mal. The attacks had in-
creased in number, his intellect was getting impaired, and he had begun
to get a slightly idiotic look. Brown-Séguard's preparation profoundly
depressed his system, and did not lessen attacks. Picrotoxin 40 gr.
four times daily had a rapid effect. In a few weeks the attacks ceased. The
remedy was gradually withdrawn, and after five years the attacks had
not recurred, and the boy did well at school.

COBALTO-NITRITE OF POTASSIUM.

recommends cobalto-nitrite of potassium (Sadtler's formula = Co₂(NO₂)₆
K₆[2H₂O]) in cases where it is desirable to lower arterial tension or to
produce any of the physiological effects of the various nitrates now in use,
and to sustain these effects for some time. The author has found the
effects more lasting and unaccompanied by fulness, throbbing, or pain in
the head when tried in cases where nitro-glycerine had caused these symp-
toms. The dose usually given was half a grain every two to four hours.