4. Rapid development of belladonna poisoning from the use of sulphate of atropine eye-drops. (*See also* p. 433.)

(*Lancet*, Jan. 8, 1898.) The patient had been ordered eye-drops, 4 gr. of sulphate of atropine to 1 oz. of distilled water, 2 drops to be used every four hours. The day after using the drops she had dryness of the tongue, lips, mouth, and throat, and great craving for drink, and the pupils were widely dilated. She also suffered from some oppression of the heart and giddiness, which was increased after taking food. Cases of extreme susceptibility to the action of belladonna are by no means rare. In this particular case, however, the curious feature is the rapidity with which the symptoms developed after the absorption of the drug from the conjunctiva.

5. Salicylate of cinchonidine has frequently been employed as a tonic and antiperiodic in neuralgia, rheumatism, sciatica, etc., and it has ordinarily been administered in doses of 5 gr. every two hours. **Walcott**, of Massachusetts, records a case of untoward effects, resulting from the use of 10 gr. of this drug, ordered in a single dose. The patient had been suffering from neuritis, affecting the median nerve of the right arm. An hour after taking the first powder, at 10.30 a.m., she felt "queer" (*Therap. Gaz.*, Sept., 1898), her head buzzed, and some nausea was present. At 2.30 she took another powder and again had headache, accompanied with marked vertigo, profuse lachrymation, with slight blurring of vision and severe pain in the face, jaw, and limbs. The bladder soon became affected; urination was frequent, only a small amount of clear, colourless urine being voided. Later the face became swollen, while the nausea persisted. After falling asleep at midnight there was gradual diminution of trouble, although the increased frequency of micturition persisted for ten days. The above symptoms combine some of those of overdoses of salicylates, and of quinine; it is therefore curious to note that no mention is made of buzzing in the ears, nor of albuminuria or hæmoglobinuria.

6. Sulphonal.

Although toxic symptoms have often been noted in connection with overdoses of sulphonal, they have usually been regarded as causing inconvenience rather than danger. A fatal case of sulphonal poisoning has, however, been recorded (*Berl. klin. Woch.*, Sept. 26, 1898) in a woman, aged thirty-two. The symptoms commenced thirty-six hours after the administration of sulphonal had been stopped, and consisted at first of pains and vomiting, and later, of paralysis and hæmatoporphyrinuria. Besides ataxia, there was paralysis of the arms and legs. The hæmatoporphyrinuria occurred eight days after the onset of the toxic symptoms, and later, albuminuria and other evidence of toxic nephritis appeared. The chief change, apart from the toxic nephritis, consisted in the degeneration of the heart muscle. **Wien**, who records this case, considers that there is danger in the continuous employment of sulphonal, and believes that, if frequently given, intervals of four or five days should be allowed. He considers that sulphonal is a cumulative poison, and that when any toxic symptoms are present, excretion should be favoured by diuretics, while camphor should be used to avert the danger of cardiac failure.

7. A case of poisoning by **convallaria majalis** is recorded in the *Therap. Gaz.*, Feb., 1898. The patient, a child aged two, was given nearly a teaspoonful of liquid extract of convallaria majalis by mistake. An hour later the child was extremely restless, with continuous trembling of the arms and legs and with general convulsions. She could with difficulty be roused from her condition of stupor. The pupils were moderately dilated, the temperature was subnormal, the pulse extremely irregular and, when it could be counted, 140. Respirations were shallow and superficial; the face slightly flushed. There were no signs of gastro-intestinal irritation, nor of diuretic or diaphoretic effect. With symptomatic treatment the child gradually regained her normal condition. Cases of poisoning with this remedy have so rarely been recorded that the foregoing account is of considerable interest.

8. Local effects of iodoform.

Dry iodoform gauze has been credited with the production of attacks of bullous dermatitis of the hands. The appearances in many cases have been attributed to gout, and relief is afforded by the firm application of bandages to the fingers, with boracic ointment (*Lancet*, Feb. 5, 1898).

B.—NEW REMEDIES.

I.—Local Anæsthetics.

9. Holocaine.—The introduction of this local anæsthetic, and its employment as a substitute for cocaine and eucaine, were referred to in the "Year-Book of Treatment for 1898." It is a derivative of para-phenetidin, from which are also derived phenacetin and lactophenin. It is insoluble in cold water, but readily soluble in alcohol and ether. The chlorhydrate of holocaine is, however, slightly soluble in cold water, and its aqueous solution is neutral and undergoes no change on prolonged boiling.

Hinshelwood (*Brit. Med. Journ.*, Sept. 3, 1898) has employed a 1 per cent. solution in a large number of cases, and he finds that it produces complete anæsthesia of the cornea and conjunctiva in from fifteen to thirty seconds after instillation. The anæthesia lasts about ten minutes. It is preceded by a slight feeling of burning, which rapidly passes off. It causes no alteration in the size of the pupil, no disturbance of accommodation, no alteration in the tension of the eye, and the corneal epithelium retains its normal appearance. Shortly after instillation it produces slight hyperæmia of the bulbar and palpebral conjunctiva, which rapidly passes off. In the discussion which followed this paper, **Argyll Robertson** said that he had used a 2 per cent. solution and had found it infinitely inferior to cocaine as a local anæsthetic, and, commenting upon this remark, Hinshelwood laid stress upon the importance of employing fresh preparations. He said that he used a solution which was made up fresh every week, and found that it would not keep longer than a fortnight.

Hotz (*Journ. of the American Med. Assoc.*, Nov. 13, 1897) says that the instillation of holocaine always caused more or less smarting or burning, which, however, only lasted about half a minute. It produced redness of the conjunctiva, which persisted during the whole period of anæsthesia. Complete anæsthesia of the cornea was noted within one and a half to two minutes; after six minutes sensibility began to return, then a second instillation prolonged the anæsthesia for another five minutes. It would appear that the anæsthetic effect of holocaine can be kept up by repeating the instillation every five minutes. Holocaine has no effect in causing dilatation of the pupil and no effect on accommodation. Hotz, as the result of several experiments, concludes that the anæsthetising effect of cocaine, 2 per cent., is more thorough and penetrating than that of holocaine 1 per cent. The effect of holocaine is very quick and superficial, and while it is a very useful local anæsthetic for the removal of foreign bodies from the cornea or for operation on the conjunctiva, cocaine is the more trustworthy anæsthetic for deeper operations, especially for those which involve iridectomy and cataract extraction.

10. Orthoform has been employed in the local treatment of painful ulcerations with special reference to the upper air-passages by **Young** (*Brit. Med. Journ.*, Feb. 5, 1898). After giving an account of the chemical composition of this new synthetic product and showing its relation to cocaine, he gives some details of cases in which he has used the remedy as a local anæsthetic. It is best employed in the form of a spray. Its composition is 5 grains in 100 minims of equal parts of rectified spirit and water. The spirit evaporates shortly after contact, leaving the precipitate of powder evenly distributed over the affected area. He employed this drug chiefly in painful ulcerations of the upper respiratory tract, and he found that it was devoid of toxic effects although occasionally it produced some slight burning for a few minutes after its application. He thinks it is probable that it may replace cocaine when long anæsthesia of ulcerated surfaces is wished for, while on the other hand cocaine would probably be employed when short insensibility of an intact mucous membrane is desired.

II.—ANTIPYRETICS.

11. Kryofin.—Reference was made to this new drug in the "Year-Book of Treatment" for 1898, p. 456, and the account then given showed that it had some antipyretic power. It had been employed since by **J. H. Curtis** (*Therapeutic Gaz.*, May, 1898), who finds that even when no reduction of temperature follows its employment there is absence of increase of blood-pressure. It is rapidly absorbed and rapidly eliminated, and he states that it controls neuralgic pains in a marked and sometimes almost magical manner, and in some persons produces a tendency to sleep. Kryofin is one of the coal-tar derivatives, and it is saponified with hydrochloric acid. The dose administered is eight grains. Curtis states, that notwithstanding its power of reducing temperature, he is of opinion that except in occasional cases the use of agents that reduce temperature by lessening the oxygen-carrying capacity of the blood is scarcely good treatment in pneumonia. In most of his cases the drug was employed for the relief of pain—indeed, the analgesic properties and the rapidity of action in all cases of a neurotic character, are the features upon which he lays the greatest stress.

12. Euchinine, which was introduced as a substitute for quinine, was mentioned favourably in the "Year-Book" for 1898.

St. George Gray (*Brit. Med. Journ.*, Feb. 26, 1898) gives his experience of this drug in malarial fevers, and he finds it superior to quinine in being tasteless and in requiring a smaller dose to reduce the temperature. Contrary to the statements of Von Noorden, he finds that ten or fifteen grains of euchinine are as efficacious as from twenty to thirty grains of quinine sulphate, and that it nearly always causes buzzing in the ears, if not other symptoms of cinchonism. He lays stress upon the smaller dose and upon the tasteless character, considering the latter the chief advantage over quinine.

13. Methylene blue in malarial fever.

Methylene blue has been recommended in cases of malaria,

where quinine had proved useless, or where there was intolerance of quinine. **Cardamatis** has used it in a very large number of cases, apparently with success. In some of his cases he has found it advisable to use both methylene blue and quinine, but in the large majority he employed methylene blue alone. He found that the drawbacks included staining of the tongue and lips, and sometimes a slight amount of cystitis. He considers that patients are not only cured of existing malaria, but that they are also rendered immune, so that they may continue to reside in malarial districts with but little danger of subsequent attacks. The daily dose was from 10 to 12 grains for adults, and the drug was administered in intermittent fever some ten hours before the beginning of the paroxysm.

14. Olive oil in the treatment of typhoid fever.

Olive oil is not commonly credited with antipyretic properties. Indeed, apart from a knowledge of its domestic employment as an article of diet, or as a mild laxative for infants, it may be doubted whether medical men consider it seriously; still **Owen Paget**, of Freemantle, Australia (*Lancet*, Nov. 27, 1897), claims to have treated a large number of patients (well over 100) without a single death, and he attributes this result largely to the use of salad oil. This he has given as an injection by the bowel, a large breakfastcupful (from a quarter to half a pint) being used for the first four or five days, at intervals of twelve to twenty-four hours, and he claims that it reduces the temperature and soothes the patient. After the fifth day he administers the oil every second day. When the injection has no result and the temperature goes up, he gives the salad oil by the mouth, a large breakfastcupful at a time, and repeats this dose after twelve hours if there has been no evacuation. The treatment appears to depend entirely upon its power of emptying the bowel. Owen Paget does not, however, indicate the course of action to be followed when the individual is already suffering from much diarrhœa.

III.—Antiseptics.

15. Chinosol, a member of the quinoline group, with reputed antiseptic, disinfectant, and deodorant powers, has been studied by **Hobday** (*Journ. Comp. Path. and Therap.*, March, 1898). The pure powder, applied to wounds, causes great pain, but in dilute solutions (from 1 in 1,000 to 1 in 60), it can be used as a disinfectant for the hands and skin, though the stronger solutions are very apt to discolour instruments. Although concentrated solutions could be safely applied to the unbroken skin of the dog, toxic symptoms were readily produced in the cat. Where subcutaneously

injected, the chief toxic symptoms were sneezing and coughing, an increased flow of thick, ropy saliva, subnormal temperature, staggering gait, prostration, and ultimately death from failure of the heart's action.

16. Protargol has of late been gaining ground in the treatment of many forms of ophthalmia, and it has recently been used as a substitute for nitrate of silver in ophthalmia neonatorum, and also in some cases of gonorrhœal ophthalmia and acute conjunctivitis (*Boston Med. and Surg. Journ.*, Aug. 25, 1898). The strength employed varies from a 10 per cent. to a 2 per cent. solution. The former causes flushing of the eye and discomfort, while the latter can be used without cocaine. The solution is gently applied to the conjunctiva with a pledget of cotton-wool. The 2 per cent. solution seems to have given the most satisfactory results. In acute conjunctivitis, however, the protargol has been employed in $\frac{1}{2}$ per cent. solution. Most of the cases thus treated recovered promptly, but perhaps not more rapidly than they might have done under some of the more commonly used remedies. The advantages claimed for protargol are that it produces less irritation, and that there is less tendency to the formation of fibrinous coagula.

Neisser describes this drug (*Therap. Gaz.*, March, 1898) as a chemical combination of silver with proteid, which forms a yellowish, fine powder, readily dissolved by being shaken with water. It contains 8·3 per cent. of silver, and its solution is not precipitated by dilute sodium chloride or hydrochloric acid, and it is therefore likely to penetrate deeply into the tissues. Neisser has employed protargol in gonorrhœa, and he employs solutions of a $\frac{1}{4}$ per cent. at the beginning of the treatment, and increases the strength until 1 per cent. solutions are being used. He asserts that he has never had from any other drug such rapid, satisfactory, and safe cures.

17. Iodoformogen is described as being a combination of iodoform with albumin in the form of a bright, yellow powder, which is practically odourless, and can be sterilised at 100° C. **Kronmeyer** (*Berl. klin. Woch.*, May 7, 1898) states that he has used it as a substitute for iodoform, but that, like the latter, it may produce eczema. He believes it to be the best available dusting powder for wounds.

IV.—Drugs Acting on Nerve Centres.

18. Synthetic analgesics.

The discussion at the meeting of the British Medical Association at Edinburgh on "The Therapeutic Value of Recent Synthetic Analgesics: their Benefits and Attendant Risks," was introduced by **Stockman** (*Brit. Med. Journ.*, Oct. 8, 1898) with a

lucid account of the chemical relationship of these substances, followed by a summary of their uses and their dangers. He indicated the risks of producing disintegration of the red blood corpuscles, and owing to the smallness of the dose of acetanilide, and its pronounced action on the blood, gave preference to antipyrin and phenacetin. He also spoke favourably of lactophenin. **C. D. F. Phillips** thought antipyrin, antifebrin, phenacetin, and exalgin of greater service than many of the newer synthetic analgesics; he considered salophen, phenocoll hydrochloride, apolysin, and methylene blue of high therapeutic value; agathin was slow and unreliable, and many others were unnecessary, though they might be used with comparative safety as substitutes for better remedies.

19. Methylene blue. (See also pp. 441 and 450.)

A summary of the actions of methylene blue is to be found in the *Revue de Thérap. Médico-Chir.* of April 1, 1898. In this, three distinct properties are attributed to methylene blue: (1) It is a colouring agent; (2) it acts as a microbicide or disinfectant; (3) it possesses distinct analgesic properties. These latter have been attributed to the transformation of oxyhæmoglobin into methæmoglobin. As an analgesic it has been employed for facial and sciatic pain; also for rheumatic pains, angina pectoris and migraine. Its chief disadvantage is the discoloration of everything with which it comes into contact, and for this reason as well as on account of its disagreeable styptic taste, it is preferably given in the form of pill or cachet.

The pains of ataxia have been treated by **Lemoine** with methylene blue, and he believes that this remedy has led to great diminution in the intensity and frequency of the pains (*Therap. Gaz.*, Feb., 1898). He thinks that the greatest relief is given in the darting pains in the limbs, and in the sensation as of a tight band drawn about the patient. He asserts that the effect of methylene blue is very rapid, its discoloration of the urine being noted between two to three hours.

20. Mydrin.

The claims of this mydriatic were referred to in the "Year-Book" of 1898, pp. 368, 455. **Stephenson** (*Lancet*, July 2, 1898), as the result of experiment with a 10 per cent. watery solution, concludes that it causes a moderate dilatation of the pupil, without involving the function of accommodation. The dilatation occurred somewhat slowly, the average time being 29·35 minutes, it lasted on an average a little more than three hours, and it was not accompanied by discomfort or irritation.

21. Euphthalmine hydrochlorate is mentioned in Merck's

Annual Report for 1898 as possessing a powerful mydriatic action which, however, is less intense and slower in the aged than in the young. Its instillation is not attended by pain nor by other unpleasant secondary effects, and the power of accommodation is less affected than by homatropine. **Winselmann** (*Klin. Monats. Blätt. f. Aug.*, July, 1898) employs a 5 per cent. solution which causes a maximum of mydriasis in thirty-two minutes, while a 10 per cent. solution produces a maximum dilatation in twenty-three minutes. This dilatation of the pupil lasts from three to three and a half hours, and the normal size is ultimately resumed in about seven hours.

V.—Cardio-Vascular System.

22. Aconitine, benzaconine, and **aconine,** the alkaloids of aconite, form the subjects of an interesting paper by **Cash** (*Brit. Med. Journ.*, Oct. 8, 1898) dealing mainly with the pharmacology. Aconitine is the most toxic, and it possesses the strongest antipyretic power. Benzaconine, although it reduces the blood pressure, is not lethal owing to its action on the heart, but rather from respiratory failure. Aconine strengthens the ventricular systole and opposes the asequence and inco-ordination which aconitine so actively produces. Cash suggests that, if it can be produced in sufficient quantity, it might be of value in some conditions of accelerated and irregular heart's action. He states that many samples of "aconitine," especially of German manufacture, have consisted to some extent of benzaconine and aconine, which would account for some of the different results obtained by other observers.

23. Periploein.

Periploein is a glucoside, derived from the bark of periploea graeca. **Burzinski** found that it slowed the action of the heart, while it increased the blood pressure; with a larger dose the blood pressure still remained high, but there was increased frequency of pulsation, while with still larger dose the pulse became irregular, and the heart stopped suddenly, the blood pressure rapidly falling. **Levaschoff** (*Vratch*, No. 11, 1898) found periploein peculiarly suitable for hypodermic injection, since it is soluble in water and causes no severe irritation at the site of injection. Having determined the maximum daily dose (0·001 gr.) by experiment, he proceeded to investigate its actions. By sphygmographic tracings he found that for an hour after injection the blood pressure was raised, while the rapidity of the heart's action was diminished The area of cardiac dulness was not materially altered. It produced diuresis in heart disease, but not in cases of dropsy dependent upon kidney or liver changes. If