PART III.

SPECIAL REPORTS.

REPORT ON

MATERIA MEDICA AND THERAPEUTICS.*

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Saponin.—About six years ago Professor Kobert announced that commercial "saponin" was not a homogeneous compound, but, as a rule, consisted of at least four different bodies, two of which were inert while the other two were very poisonous (*Pharm. Journ.*, [3], xvi., 366). Since that time the investigation has been continued in the Pharmacological Institute at Dorpat, and the sixth part of the "Arbeiten," recently issued, contains two exhaustive papers, by Nicolai Kruskal, upon "Some Saponin Substances" and "*Agrostemma Githago*, L." As these papers will probably close the investigation for the present, Professor Kobert has taken the opportunity to summarise the conclusions to be drawn from the results as far as it has gone. In the first place he expresses the opinion that the idea of a saponin as described usually in the text books has no pharmacological foundation, and at most can only have a collective application. But in price lists it should be replaced by "quillaia sapotoxin," "quillaic acid," &c., or if the name "saponin" be retained, the drug from which it has been prepared and the method of preparation should be shortly indicated. In the so-called "saponins" the chemist apparently has to do with different series of bodies, the composition of each series being represented by a general formula. One of these formulæ, now published for the first time, is $C_nH_{2n-8}O_{10}$, and represents a series of which at least three members have been recognised. The best known of these is the "saponin" of Stutz, $C_{19}H_{30}O_{10}$. The lowest member of this

* This Report is based upon an article by the writer in the "Year-Book of Treatment" for 1892.

series, which gave on analysis figures corresponding to $C_{17}H_{26}O_{10}$, shares this formula with the crystalline "syringin," which Körner identified as oxymethylconiferin hydrate. The amorphous substance of this composition prepared by Kruskal agrees with syringin in being a glucoside and giving a characteristic colour reaction with sulphuric acid, but whether other analogies between the two exist has not yet been determined. But one observation of the greatest interest is that it appears that several substances of this class exist which give the same results on analysis and behave similarly in all their chemical reactions, but which when tested pharmacologically show an enormous difference in the intensity of their toxic action. One of them, the "agrostemma sapotoxin," differs also physiologically from the other saponins in being absorbed by the subcutaneous tissue and by the larger intestines. This is considered to be of great hygienic importance in presence of the fact that in Russia the admixture of a certain proportion of corn cockle seed with corn is allowed upon the plea that when ground it improves the appearance of the flour. Professor Kobert considers that the continuance of this practice should be permitted only on condition of the previous removal as far as possible of the black husk and poisonous embryo.—(*Pharm. Journ.*, June 27, 1891.)

Cocaïn and Mercury Compounds.—A delicate reaction between cocaïn hydrochlorate and calomel has been observed by M. Schell (*Journ. Pharm. Els. Loth.*, Jan., p. 8). If a trace of cocaïn hydrochlorate be mixed by means of a dry glass rod with a very minute quantity of calomel, and the mixture be breathed upon, the moisture that condenses is sufficient to cause it to blacken immediately. No other alkaloid has been found to give the same reaction, but atropin and calomel acquire a similar coloration in boiling water or alcohol and water. It is curious to note, however, that in the case of atropin it occurs with the free alkaloid and not with a salt, whilst in that of cocaïn it occurs with a salt and not with the free alkaloid. Herr Bruner also has called attention to the incompatibility of some preparations for outward application, in which a cocaïn salt is ordered in conjunction with a mercurial compound (*Apot.-Zeit.*, Feb. 11, p. 86). An ointment of mercuric oxide and cocaïn hydrochlorate, for instance, is ordered in ophthalmic practice, but after being kept for a time the anodyne effect of the ointment gives place to a pronounced caustic action, due to the conversion of mercuric oxide into oxychloride. An ointment of cocaïn hydrochlorate, silver nitrate, and vaseline, sometimes ordered

as a dressing for wounds, is also liable to undergo alteration through formation of silver chloride, but it is pointed out that this change can be retarded by thoroughly mixing the solution of silver nitrate with the vaseline before adding the cocaïn hydrochlorate.—(*Pharm. Journ.*, 1891.)

ANTIPYRETICS.

Action of Antipyretics.—The theory as to the mode of action of antipyretics is of great practical interest. The action of antipyretics may be supposed to be due to the limitation of the oxidation processes and consequent lowering of heat development, or to an increase in the heat radiation from the surface of the body. Moreover, they may have a purely local action—*i.e.*, on the cellular tissue, or they may influence the nerve centres regulating the development or radiation of heat. Messrs. Sawodowsky and Podanowsky consider that they have proved that the lowering of temperature produced by antipyrin and antifebrin is attributable exclusively to their influence upon the brain-centres regulating the temperature, which occur in the corpus striatum (*Apot.-Zeit.*, Feb. 11, p. 87). The authors, in an experiment, cut the brain of an animal through close behind the corpus striatum and thalamus opticus, so as to isolate the organism from the heat centres, while the connection with the respiration and vaso-motor centres was retained. Although the animal so treated lived for some time and the arterial blood pressure and breathing remained unaltered, the body temperature fell continuously. Even injections of the most powerful pyretics, such as putrescent matter, caused not the slightest rise of temperature, although all the other symptoms of putrescent infection were present. The skin temperature also remained entirely unchanged, although in the case of normal animals this rises considerably after the injection of antipyretics. An apparent exception was noticed in the case of quinine hydrobromide, but this was attributed to the known action of bromine. The conclusion drawn by the authors is that the action of quinine salts, resorcin, and thallin, in lowering the temperature is dependent upon their specific influence upon the temperature-regulating centres situated in the anterior part of the brain.—(*Pharm. Journ.*, Feb. 28, 1891.)

Dr. Gottlieb points out that by calorimetric determination of the total loss of heat of an animal, at a given temperature, we can also determine the value of its heat-production. He arrives at these conclusions :—

Quinine depresses in rabbits the production of heat. The diminution in normal animals amounts to from 8 to 18 per cent.; in pyrexia induced by puncture of the brain, to 40 per cent. Simultaneously it lessens the loss of heat.

Antipyrin lowers the temperature exclusively by bringing about increased loss of heat. There is no diminution in the production of heat; *per contra*, it, in small doses, at first increases the production of heat. The rise in temperature after puncture of the brain is a regulative disturbance, and the reason why antipyretic drugs have so little effect upon healthy men and animals is the perfection of their heat-regulating mechanism.

The results of experiments upon animals agree with the clinical indications drawn at the bedside. Whenever our main object is to lower high temperature quickly, and as safely as possible, we choose a member of the antipyrin group. For long-continued antipyretic treatment, on the contrary, we give the preference to quinine.—(*Archiv. f. exp. Pathol. u. Pharm.*, xxviii., p. 167.)

Phenocoll Hydrochlorate.—This body, an ally of phenacetin, is an addition to the group of antipyretic and anti-rheumatic remedies; and has been reported upon by Dr. Hertel (*Deut. med. Wochenschr.*, April 9, 1891). It is a white powder, in small crystals, with a bitter taste, and soluble in sixteen parts of water at 62° F. According to Kobert it is not poisonous to animals, and has no deleterious effects on the blood, while von Mering found that 22 grains produced no symptoms in a rabbit, and that in pneumonia and typhus 15 grains acted as a trustworthy antipyretic, reducing temperature about 2° C., and never causing collapse or cyanosis. The amount of sweating was about the same as after large doses of antipyrin. Of phenocoll, a dose of 15 grains equals in its antipyretic action 23 to 30 grains of antipyrin, and 12 to 15 grains of phenacetin. Doses of 7 to 15 grains acted well as an antineuralgic. Hertel gave it in doses of 7 to 15 grains in cases of phthisis and rheumatism. The following is a summary of his results:—In phthisis, single doses of 7 grains lower the temperature about $\frac{1}{2}$ ° C. for a short time. Doses of 7 grains given hourly for three hours reduce the temperature about 1° C., but not with certainty; the reduction lasts only a short time. Doses of 15 grains cause reduction of temperature, 1° to 1 $\frac{1}{2}$ ° C. in a few hours, the reduction generally lasting about two hours. Seventy-five grains given during twenty-four hours generally keep the temperature normal. The subsequent rise of temperature is regular, and unaccompanied by rigors or sweating. In

acute rheumatism the same dose keeps the patient free from pain, but scarcely reduces the temperature, which only falls when the joint affections improve. It has no effect in gonorrhœal rheumatism. The urine, after about 75 grains have been taken, becomes brownish-red or dark brown in colour, becoming deeper-coloured on exposure to the air. On adding solution of perchloride of iron, a dark colour is produced, which clears up somewhat with strong sulphuric acid, but does not disappear entirely, and by transmitted light shows a peculiar greenish colour. Phenocoll is excreted very quickly, as this reaction is not obtained for more than about twelve hours after the last dose. No disturbance of the heart, respiration, or digestion was ever observed. It should not be kept in watery solution, as it decomposes slowly. Hertel states that he was very favourably impressed with the general results of its use, and advises further observations.—(*Brit. Med. Journal*, Suppl., May 2, 1891.)

Phenacetin in Influenza.—Dr. Clemow (*Brit. Med. Journal*, June 27, 1891) fully corroborates the testimony of other observers as to the excellent effects of phenacetin in epidemic influenza. He usually gives 5 to 10 grains, either in cachets or suspended in milk, to be repeated in an hour if the pains are not fully relieved, and then every four hours until further directions. He is fully convinced of the superiority of this drug over antipyrin and salicin, and has met with no bad symptoms from its use. The greater rapidity with which the pains are relieved is very striking, and phenacetin takes rank as one of the most valuable analgesics.

ANTISEPTICS.

Benzoate of β -naphthol.—The insolubility of the higher aromatic compounds has till recently been a great obstacle to their study as antiseptics. The naphthols, especially naphthol β , have been for some time administered as intestinal antiseptics, but it was soon found that a compound of naphthol β with salicylic acid, introduced under the name of bethol, was more efficient. This substance varied considerably in composition, and was also inadmissible when on account of renal disease salicylic acid was contra-indicated.

MM. Yvon and Berlioz have prepared a benzoate of naphthol, which is soluble in alcohol or chloroform, feebly soluble in water or ether. This compound, when introduced into the intestine, breaks up into naphthol β (which remains in the intestine) and benzoic acid, which is eliminated by the kidneys in the form of alkaline salts and alkaline hippurates—(1) It is very slightly poisonous;

(2) it is an antiseptic as powerful as its congeners; (3) it encourages diuresis, the absorbed portion being rapidly eliminated by the urine; and (4) it can be given in large doses, but it is advised to give small and frequently-repeated doses rather than single large quantities. More than a drachm daily has been administered to an adult. (*Brit. Med. Journal*, Suppl., Nov. 7, 1891.)

Dr. F. W. Burton, in a paper on Putrefactive Decomposition in the Intestinal Tract (*Brit. Med. Journal*, April 4, 1891), cites several cases of typhoid fever and of tuberculous ulceration of the bowel, in which β naphthol was given with marked benefit—2 to 8 grains every few hours. It checked the diarrhoea and lessened the offensive odour of the stools.

Iodphenin is formed by treating with iodine phenacetin, to which some hydrochloric acid has been added. It can be obtained in steel-blue crystals, and is almost insoluble in water, but soluble in alcohol. Herr Scholvien brought iodphenin before the Berlin Pharmaceutical Society as a compound possessing extraordinary germicide properties. It is claimed that five minutes' contact with a 1 in 5,000 solution of iodphenin renders *Staphylococcus aureus* incapable of further developing.—(*Pharm. Journal*, May 30, 1891, from *Apot. Zeit.*)

Sulphite of Zinc.—Twenty years ago, in a paper read before the British Pharmaceutical Conference at Liverpool, Professor Tichborne called attention to the possible value of zinc sulphite as an antiseptic (*Pharm. Journal*, [3] i., 351). Recently he has again suggested it as a material for the preparation of antiseptic dressings, and Dr. Heuston (Adelaide Hospital, Dublin) reports that for this purpose he has found it superior to sal alembroth, it being non-poisonous, non-irritative, and highly antiseptic (*Brit. Med. Journal*, Nov. 8, p. 1064). Professor Tichborne states that zinc sulphite is best prepared by mixing in solution six parts of zinc sulphate and five and a quarter parts of sodium sulphite. The reaction takes place slowly, but goes on to completion, the new salt, which forms as a white crystalline precipitate, being very insoluble in water, though soluble in excess of sulphurous acid. Dried at 100° C., it has the composition represented by the formula $\text{ZnSO}_3 \cdot 2\text{H}_2\text{O}$, but if only dried at the ordinary temperature it contains another molecule of water. In contact with water it undergoes a slow but regular oxidation, which in an experiment with a saturated solution was complete on the eighteenth day. Zinc sulphite can be used for the saturation of any fabric, such as gauze or lint, without the

intervention of an adhesive material. The fabric is first boiled with water, to cleanse and sterilise it, after which a boiling solution of zinc sulphate and sodium sulphite in equivalent proportions is poured upon it, and when thoroughly mixed and saturated, the whole is allowed to stand for twelve hours. The zinc sulphite is said to be deposited in and about the fibres of the fabric in microscopic crystals, soft and even unctuous to the touch. The fabric is then passed under rollers submerged in water to remove traces of sodium sulphate. It is suggested that this kind of dressing might be dyed with an organic pigment to distinguish it from others, and for the purpose of indicating the progress of the discharges by the action of liberated sulphurous acid on the colour.—(*Pharm. Journal*, Nov. 20, 1890.)

Creolin.—A number of instances are on record in contravention of the asserted non-poisonous qualities of creolin. Some important evidence as to the action of creolin on the human subject may be gathered from a thesis on that compound published at Breslau during the course of this year. Dr. Bitter, the author, notes that creolin has already been used in more than 2,000 midwifery cases at Breslau. As appears to be the case with nearly every new compound of the kind, the results, according to Drs. Born and Bitter are most encouraging. In four of the midwifery cases, however, symptoms of poisoning occurred during the administration of a course of creolin injections. Three of the patients were suddenly seized with feelings of restlessness, anxiety, nausea, darkness before the eyes, and a tendency to syncope. The most peculiar feature in these cases was a strong flavour of tea or smoke in the mouth, of which all the patients complained. This symptom lasted for a long time, whilst the nausea, &c., disappeared immediately upon the discontinuance of the vaginal injections of creolin. The fourth case was more severe; the patient suffered from great restlessness and prostration for several days after the injections were left off. About thirty-six hours after the beginning of the attack the urine, drawn off with the catheter, was very dark and strongly albuminous. Within a few days these symptoms of acute nephritis disappeared. Dr. Bitter advocates creolin as superior to other disinfectants on account of its "relatively" (*sic*) non-poisonous qualities, its excellence as a deodoriser, and its blandness when applied to skin, mucous membranes, and wounds. It neither dries the vaginal mucosa nor causes any contraction of the canal. Creolin has no special hæmostatic action. Dr. Bitter finds that there are dis-

advantages in creolin, as the emulsions employed for injections are opaque, and the preparation of creolin usually on sale appears to be unstable.—(*Brit. Med. Journal*, Dec. 13, 1890.)

Hydro-naphthol has been before the profession for some time, but its powers as a germicide are differently estimated by different observers.

Dr. T. H. Bryce (*Brit. Med. Journal*, Nov. 22, 1890) has investigated its action in the Bacteriological Laboratory, Glasgow. His experiments were all made upon one organism, *Staphylococcus pyogenes aureus*, and with a solution of hydro-naphthol in rectified spirit and glycerine. The pure drug is insoluble in water, and this is undoubtedly a disadvantage. He concludes that, when dissolved as above, it is a powerful antiseptic agent, in a strength of 1 in 400.

The standard solution 1 in 100 is thus made:—

Hydro-naphthol	...	...	...	1 part	} 1 part
Rectified spirit	...	...	...	10 parts	
Glycerine	...	...	...	...	9 parts

Aristol, a proposed substitute for iodoform, does not appear to have attracted much attention. The contradictory experiences that have been reported may, perhaps, be partly explicable by variation in its quality. Herr Reuter finds that some specimens of aristol (= dithymol diniodide) contain alkaline iodide and free iodine. But the question arises whether an absolutely pure preparation is advantageous, for it would seem that pure aristol is so stable that it would be less likely to act as a bactericide than a preparation rendered unstable by the presence of more or less free iodine or alkaline iodide.—(*Pharm. Journal*, from *Apot. Zeit.*, Jan. 28, 1891; cf. Pollak, *Therap. Monatsch.*, December, 1890.)

Apomorphin and Apocodein.—Dr. Murrell (*Brit. Med. Journal*, Feb. 28, 1891) has made some interesting observations upon the value of these drugs as expectorants in the treatment of chronic bronchitis. Apomorphin can be given by the mouth in comparatively large doses ($1\frac{1}{2}$ to 2 grains three times a day), without exciting vomiting or inconvenience. It may be applied successfully in the form of ointment ($\frac{1}{3}$ gr. to 3 i.), and is invaluable in the bronchitis of children.

A neutral solution of apocodein can be injected hypodermically ($\frac{1}{2}$ grain) without causing local irritation. It rarely produces nausea or vomiting, and is an effective expectorant. From 3 to 4 grains may be administered daily with perfect safety.

Diuretin has attracted some attention. It is now generally understood to be merely a mixture of theobromine-sodium and sodium salicylate. It is very unstable, and is decomposed by all acids, even by the CO_2 of the atmosphere.—(*Lambert*.)

Dr. Geisler speaks well of the drug, and states that it raises the blood pressure (*Berlin klin. Wochensch.*, April, 1891), while Dr. Drozdovsky, of St. Petersburg, sums up by saying that diuretin (a) has no influence on the heart, (b) it is very unreliable as a diuretic agent, and (c) cannot advantageously be used as a substitute for digitalis, adonis, strophanthus, and other allied remedies.—(*Brit. Med. Journal*, Oct. 10, 1891.)

The dose of diuretin required is large—viz., 5 to 7 grammes a day. The drug is expensive, and, upon the whole, its claim for recognition does not appear to be a strong one.

Sulphonal.—Dr. Stewart, of Philadelphia, states that sleep can be readily induced by sulphonal, *within a few minutes*, by the simple expedient of dissolving the dose of sulphonal in about 6 fl. oz. of *boiling water*, the patient taking the liquid as hot as can be borne.—(*Braithwaite's Retrospect*, from *Philad. Med. News*, Jan. 1, 1891.)

Cantharidin in Phthisis.—In view of the conflicting statements that have been made as to the preparation and dose of the liquid used by Dr. Liebreich in the treatment of tuberculosis under the name “cantharidinate of potash,” it may be convenient to put on record what is understood to be the exact formula, which has been kindly communicated by Dr. Schacht, of Berlin. In preparing the liquid 0.2 gram of cantharidin and 0.4 gram of potassium hydrate (or 0.3 gram of sodium hydrate) are weighed with great exactness, and heated in a flask of one litre capacity on a water-bath with about 20 c.c. of water, until a clear solution results. Water is then added quite gradually, while the heat is continued, until the mark is nearly reached, and then after cooling the whole is made up exactly to one litre with water. A litre of the liquid, therefore, contains 2 decigrams of cantharidin, and each cubic centimetre contains one-tenth of a milligram.—(*Pharm. Journal*, March 28, 1891.)

This drug is not, as in the case of “tuberculin,” open to the imputation of being a secret remedy. It, however, is liable to induce toxic symptoms, and the reports in the literature of the past year, when put together, give little encouragement for its employment in the treatment of tuberculosis. (Cf. *Brit. Med. Journal*, May 9, 23, 30, 1891.)