ACONITE (" *Wolf's bane* " ; " *Leopard's bane* " ; " *Women's bane* " ; " *Venus's Chariot* " ; " *Scorpion* " ; " *Monkshood* ; " " *Blue Rocket* "), " *Queen-Mother* " *of Poisons : its place in History, in Mythology, in Criminology ; in Botany, in Therapeutics, and in Toxicology.* By JOHN KNOTT, M.A., M.D., Ch.B. & D.P.H. (Univ. Dub.) ; M.R.C.P.I. ; M.R.I.A. ; &c.

(*Continued from page 228.*)

THE transition of such mingled items of animal and vegetable lore, through mediæval, down to modern literature, is well exemplified in Sylvester's *Du Bartas* :

> " Onely the touch of Choak-pard Aconite
> Bereaves the Scorpion both of sense and might."
>
> ——., III., xxvii., 1.

—and in Shakespeare's :

> " Though it doe worke as strong
> As Aconitum, or rash Gun-powder."
>
> 2 Henry IV., Act iv., Scene 4.

—a curious approximation of the old world to the new ; of the silent and subtle life-destroying agent which represented the most uncanny skill of classical times, to the fulgurating exterminator which was popularised with the Science and Art of the Renaissance !

The domain of *Animal Therapeutics* was, as all well-informed readers know, cultivated by the ancients with a most assiduous (and imaginative) degree of industry. It formed, indeed, during countless ages one of the most prominent articles of the healer's faith—of which recent scientific *discovery* has presented the admiring world with a feeble effort towards resuscitation. And, in this department, we find that so familiar and grateful a remedy as *cow's milk* was highly recommended as an antidote against aconite. So was the " *broth made of tripes.*" We are confidently informed, too, that the " *broth of an old Cocke* " " is most effectuall against the poison of the herbe Aconitum, but then it must be given with a little salt among." The *Castoreum*, of whose origin tales so curious were told by the ancient pharmacists and natural historians, was also included in the same rank ; for we are assured that : " soueraigne it is

for the poison of the herb Aconitum or Libard bane, in milk or faire water."

Supplementary catalogues of "antipathies" were, as might well be expected, prominently placed in the records of mediæval scientific lore; and were—as a natural consequence—highly recommended as antidotal reagents. That foremost mediæval luminary of the healing art, the Arabian Avicenna, whose *Canon* functioned for five centuries as a sort of medical Bible in orthodox professional practice, informs his readers that there is a mouse which feeds upon the root of aconite, and that "that mouse is the Treakle thereof, and being taken in the whole substance, resisteth the venome of the *Napellus*, and freeth them from all danger." These statements are corroborated by Matthiolus, the famous commentator of Dioscorides, who assures his readers that he had often found that mouse! The redoubtable Petrus Aponensis also contributes corroborative testimony on this head. He confidently informs the inquiring reader that "this Mouse which feedeth upon the roots of *Napellus* is the *Bezoar* against *Napellus*, if it be dryed and two drams of the pouder given in drinke." But, unfortunately—as ever—for the harmony of "expert" medical testimony, we have yet other three names of authoritative respectability ranged on the opposite side! Antonius Guaianerius, Petrus Pena, and Matthiolus de Lobel are, each and all three, of the opinion that it was really *not* a *mouse* at all, but a *midge*, that was intended by the great Arab physician; that it was either by a scribe's slip, or a reader's blunder, that the subsequent Greek *Textus receptus* presented a μῦς instead of the original μύια; that the root in question is really as deadly to mice as to men and to wolves; while, on the other hand, they quote the ocular evidence of "the Shepheards, and others living in those mountains of Switzerland, where the Napellus groweth in abundance," to the fact of "great store of certaine great Flies, with blewish greene heads and wings, like unto *Cantharides* feeding upon the flowers, when as they could not finde any other creature to touch or eate it; of which Flies as they say and not of any Mouse, is made an antidote most prevalent against the poison of the most venemous Spider called *Tarantula*, as also against all other Epidemicall, generally contagious diseases, and is made after this manner. Take twentie of the flies that have fed upon *Napellus*, of *Aristolochia* and *Bolearmonicke*, of each a dramme, whereof a dramme is to be

taken at a time." And we further learn that the antidote of Guaianerius against Aconite "is to be made with *Terra lemnia*, Bayberries, and Mithridate of each two ounces; xxiiii of the Flies that have fed upon *Napellus*; of hony and oyle a sufficient quantitie to make it up into an Electuary." And in this connection, Parkinson sagely remarks, in conclusion, "that *Dioscorides* and others doe write, that the *Aconitum Lycoctanum* (whereof *Napellus* is a kind and as strong) is also called *Myoctonon* or *Myophonon*, that is *Muricida*, because it killeth Mice, as well as Wolves, and therefore they could not live upon it if it would kill them." (The logic and diction of the last clause can hardly fail to strike the reader as being somewhat suggestive of Hibernian inspiration.) The statement of Pliny with regard to its telepathic influence on mice has been already quoted, and presents a curious contrast to the opinion attributed to Avicenna.

But this weirdly unique herb of the "helmet-flowers" was noticed to display a bilateral antipathetic symmetry towards certain members of its vegetable, as well as of its animal, living contemporaries. The *Anthora* possessed an established reputation as the "Counterpoison of Monkes hood"; and of it we are told by one of the grand old herbal authorities that it "groweth with or hard by the *Napellus* or *Thora*; although *Gerard* saith the contrary, and adviseth that it be not planted near the *Napellus* or Helmet flower for feare of drawing the venemos [*sic*] qualitie thereof with it." Among the many antidotes which the fertile imagination of classic antiquity provided against the life-destroying powers of aconite, we find that *Garlic* occupied an honoured place. And when we find the authority of the elder Pliny pledged to the statement that, not only "it is of power to dull and kill the force of the venomous herb Aconitum," but that also "it conquereth the soporiferous and deadly quality of Henbane: the bitings also of a mad dog it healeth, if it be applied upon the hurt . . . As for the sting of serpents verily, Garlick is exceedingly effectual if it be taken in drink; but withal you must not forget to make a liniment of it;" and even that "the very sent thereof chaseth Serpents and Scorpions away;" we can hardly feel further surprise that the Roman (and Italian) peasantry were so devoted "Garlick-eaters" as they were in the days of (Shakespeare's) *Coriolanus*. Another of these antidotes is the *Eryn ion*, or "*sea- oll* ," which also shared with garlic a fair proportion of the power against snake-poison. Indeed,

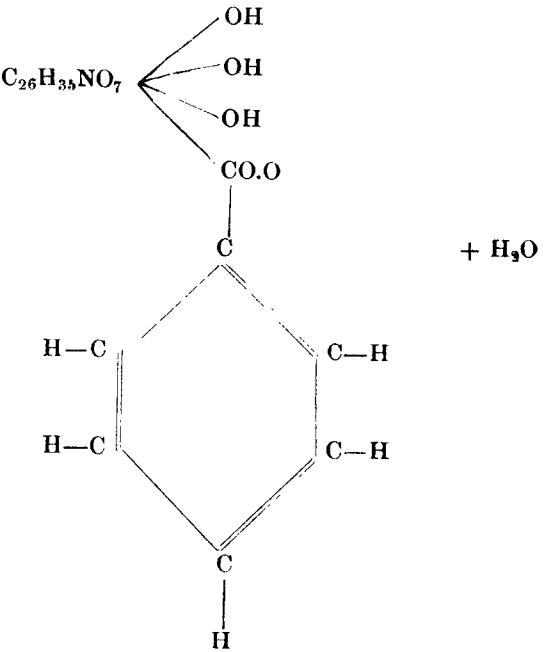
" Heraclides the Physitian " was of opinion that its root," boiled in the broth of a goose is of more efficacie than all other " against aconite, and also sundry other potent vegetable poisons. Curiously enough, Apollodorus recommended its preparation for the same purpose by having " a frog sodden withal." This mode of administration savours distinctly of the methods of the exploring vivisectionist of our own generation ; while the statement of Pliny, that " Mere wine (*merum*) not delaied is a remedy against " this and many other poisons, both of animal and vegetable origin, goes to show that the ancients displayed a distinct appreciation of the use of alcoholic stimulants in the extreme cardiac depression produced by certain toxic agents. Of another celebrated remedy we are told by the same Pliny that : " The Balsame oil, called *Balm*, is of all others most pretious . . . It danteth and mortifieth the poison of Aconitum, if it be taken with milk." Another antidote of high reputation in those classical ages of pre-scientific faith was *mulberry-juice*, of which we are told that " it is a singular counterpoison for them who have drunke either the juice of Aconit [*i.*, Libard-bane], or swallowed a venomous spider." The *house-leek* also possessed " this peculiar virtue, to resist the deadly poison of the herb Aconitum." It is interesting to notice that Pomet, the great French authority of the seventeenth century on the history and properties of " Drugs," informs his readers of the *Anthora* : " the Peasants who gather this on the Alps and Pyrenees use it with Success against the Biting of mad Dogs, and to cure the Colic ; they take it for a sovereign Remedy for those who have eat the *Thora*, or deadly *Aconite*." We are also assured by Pliny that " the greater *Sengreene* hath this peculiar vertue to resist the deadly poison of the herb Aconitum. Furthermore it is sayd, that whosoeuer carry it about them shal not be stung by scorpions."

The well-known reputation of aconite would necessarily have the effect of providing the popular imagination with numerous antidotes in times when the curative effects of faith or of fancy were rarely submitted to critical examination, and almost never to scientific tests. The separation and identification of " active principles " existed in a remote future only ; the almost miraculous accuracy and reliability of " Stas's process " had never been reached by any of the dreamy alchemists of the older centuries. As I have elsewhere shown in the present communication, the

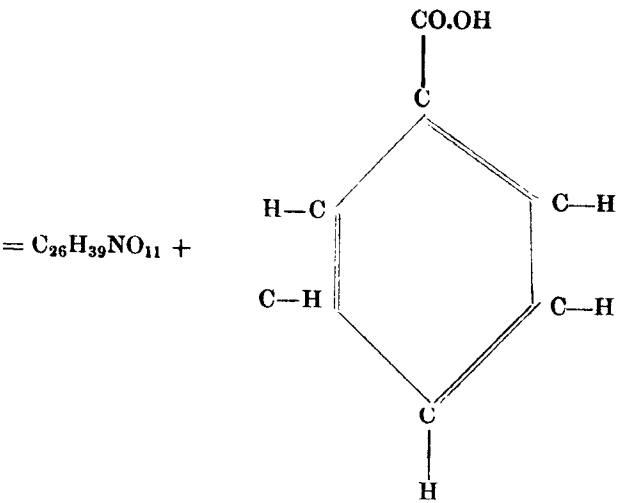
greater virulence of the root of the aconite plant was known to Matthiolus (middle of 16th century). The crystalline alkaloids have a distinct gravitational tendency in the structure of the individual plant whose juices abound in such. Aconitine, the most powerful and deadly of these agents, was separated by Brandes; but evidently in a very crude form. Hesse, in 1833, appears to have isolated the compound in a state of tolerable purity. But, from the purely scientific standpoint, all researches and results associated with aconitine down to those of Duquesnel (1870) may now be neglected. This accomplished chemist and pharmacist appears to have been the first who succeeded completely in the isolation of the alkaloid in a chemically pure state. His results led him to assign to it the formula $C_{27}H_{40}NO_{10}$. Subsequent researches, however, led to the adoption of $C_{33}H_{45}NO_{12}$ as the true representation of the aconitine molecule; this seems to be now accepted of all chemists. It appears to include the benzene nucleus, to which so large a proportion of the constitutional formulæ of the "new chemistry" owe their genesis, for it has been decomposed by certain reagents into benzoic acid and *aconine*, another alkaloid compound. And the latter has been supposed to behave as a tetraphenol of which aconitine is the monobenzoic ether. [See facing page.]

From the *A. ferox* of India has been obtained a distinct alkaloid, which has received the names of *pseudaconitine* ($C_{36}H_{49}NO_{12}$) and *nepaline* (the latter from its principal geographical source). It undergoes decomposition under the influence of corresponding reagents; but it yields a distinct alkaloid, *pseudaconine*, ($C_{27}H_{41}NO_9$) while benzoic acid is replaced by *dimethylprotocatechic acid.*

But it would seem that the heart of the physical mystery of aconitine has not even yet been successfully plucked out: its solutions used to be described as lævo-rotatory, but the recent experiments of Dunstan and Ince have announced its *dextro*-rotatory property; and a further scientific complication has been introduced by the announcement, by Richards and Rogers, of the discovery of *two isomeric* aconitines, differing widely in their toxic properties; so that it is perhaps better, in the interest of clinical (and even of toxicological) enlightenment to await the clearance of this scientific atmosphere before further discussion. One thing is certain: the last word has not yet been said on the chemical and physical structure of aconitine.

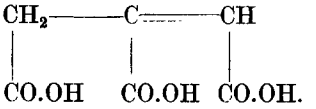


Aconitine.



Aconine. Benzoic acid.

The *aconitic* acid with which it is associated in the plant has been shown to have the composition represented by the structural formula—



—and is, accordingly, isomeric in composition with trimethylene-tricarboxylic acid. It is a somewhat curious coincidence that some of this acid has been shown to exist in the sugar cane, and in beet root.

The peculiar and interesting aspect of the flowering head of the *Aconitum napellus*, to which it owes the appellation of "monks-hood," is, of course, well known to every one who has taken even a superficial interest in botanical curiosities. In the crystalline language of the French botanist: "Les fleurs bleues forment une grappe terminale. Le calice coloré, pris communément pour la corolle, bleu, quelquefois blanc dans l'aconit napel, jaune dans autres espèces, est composé de cinque sépales très inégaux, dont le supérieur ou postérieur est en forme de capuchon. En reversant ce capuchon on découvre deux filets rappelant deux étamines, mais que ne sont que des rudiments de corolle, terminés chacun par un petit capulet. Avec un peu d'imagination, le sépale ainsi renversé peut être comparé à un char, les appendices qui terminent les deux pétales à un attelage de deux colombes, d'où le nom de *char de Vénus*."

It has been observed that although *Aconitum napellus* will grow in all soils and climes, it prefers the rocky and dry positions, so that it is found to flourish most conspicuously at the moderate elevations of mountainous regions. Accordingly, the Swiss aconite is still generally believed to be the best. Generally speaking, however, the Southern countries yield a more active specimen than do those of the North. The plant in its wild state has also been found more active than the cultivated specimen. (These facts were noted by Matthiolus, and have been confirmed by modern observation ever since his time.) Schroff has observed that it is more active before flowering than after; an interesting fact which is, pretty surely, dependent on the upward trend of the stored-up active principles from the root at the season of renewed vegetative activity.

Descending now to the records of recent botanical discovery and classification, we find De Candolle arranging 107 known

varieties of the genus Aconitum in 22 species, which are classified in 4 sections. We then have H. Baillon, the great French authority on medical botany, disposing the species of this genus which are utilised in therapeutics—also in 4 sections. Of these, the first is represented by the *Aconitum Napellus* (of Linnæus, the *A. vulgaris* of Clusius). The cognomen of *Napellus* owes its origin to the fact that the root expands "en un reservoir de sucs napiforme." The discovery, by Wallich, of the source of the Hindu poison, *Bisch*, has added the *A. ferox*. The Japanese aconite, *A. fischeri*, constitutes a still more recent acquisition to this list. The *second* is the *A. Anthora* (Linn.), which was regarded by Clusius as a distinct genus. The *third* is the *Cammarum* (*A. panniculatum*) of Lamarck, the *Lycoctonum autumnale* of the older botanists. The *fourth* is the *Lycoctonum*.

The number *four* would, indeed, almost appear to possess some specific attraction for the scientific investigators of aconite. We find Fleming, in his epoch-making thesis on this subject, not only arranging his specimens in the four sections of De Candolle, but also tabulating the symptoms and signs of their physiological action—in medicinal or poisonous doses—in four selected compartments, according to "degree of operation" (consequent on amount of dose). It is also worth noting from the same authority, writing in 1845, and as illustrative of the peculiar and dangerous uncertainty which always overshadowed the properties as well as the identity of the most deadly member of the vegetable kingdom, that: "The A. paniculatum has been adopted by the Dublin and London Colleges, on the supposition that it was the species used by Störck. I have distinctly ascertained, however, that it is totally inert; an observation which Dr. Christison has fully confirmed." The significance of the peculiar influence of Baron Störck in connection with aconite and its applications, which is so clearly implied in this quotation, must be understood by all who would have clear ideas on the therapeutic history of aconite. For the inauguration of the modern clinical employment of the preparations of this plant is undoubtedly due to the experimental researches and consequent recommendations of that eminent and enthusiastic physician. In 1762 was published his *Libellus quo demonstratur Stramonium, Hyoscyamum, Aconitum, non solum tuto posse exhiberi usu interno hominibus, verum et ea esse remedia in multis morbis maxime salutifera*, which soon came to exercise a vast influence on Continental practice. Even an approximately corresponding recognition was not established in these islands

till the best part of a century had elapsed; and this fact was in great measure due to the uncertainty associated with the connotation of the term *aconite*—as the above quotation from Fleming, I think, very clearly indicates. Störck believed that this agent had a *specific influence* on the *skin*, and on various *neuralgic* affections. He also reported great benefits obtained from its employment in many acute diseases. His remarks on *rheumatism* in this connection form an interesting item of eighteenth century pathology: "Aconiti extractum esse innocuum et valde efficax medicamentum. Parva dosi præstat id quandoque, quod alia fortissima remedia, magna dosi et longo tempore exhibita, efficere nequeant. Acre, quod circa articulos, tendines et ossa hæret, irritat nervos, excitatque summos dolores, solvitur inde, agitur in motum, et per urinam, vel alvi fluxum, vel sudorem, vel insensibilem transpirationem, ex corpore ejicitur." (In perusing such record of some of the scientific conceptions of one of the intellectual giants of a long past generation, the critical reader should charitably bear in mind that nobody then even remotely suspected that the phenomena of rheumatism were generated by the presence of a microbe, or that it would be shown at some future day to be one of the *infectious* diseases.)

(*To be continued.*)

THYMINIC ACID IN GOUT.

R. FENNER (*Pharm. Journal*) writes:—Thyminic acid is a nuclein derivative which, it is claimed, has the property of holding uric acid in solution and preventing its precipitation. It represents nucleic acid from which the uric acid yielding bases have been removed, and is the natural organic solvent of uric acid in the body. It thus prevents its deposition in the tissues in the form of salts. Minkowski gives its formula as $C_{30}H_{46}N_4O_{15}.2P_2O_5$; Kossel as $C_{16}H_{25}N_3P_2O_{12}$. It has the very interesting property of holding in solution practically its own weight of uric acid at a temperature of 20° C., while this property of retention is increased by 50 per cent. at the blood temperature of 37° C. Thyminic acid may be given internally as a powder, in an elixir, or in the form of compressed tablets. Its administration has not been attended by any toxic or untoward symptoms. It is best given with or immediately after meals, in doses of from four to seven grains.—*International Therapeutics*, Vol. II., No. 12 December, 1906.