As the experimental observations supply data for the calculation of the emissive power of the surfaces of the bars at different temperatures, a table is given at the end of the paper showing the emissive power of the surface of each bar at temperatures between 20° C. and 200° C. The values obtained agree fairly with those given by Macfarlane and Tait for somewhat similar surfaces.

V. "Preliminary Notice on the Arrow-Poison of the Wa Nyika and other Tribes of East Equatorial Africa, with special reference to the Chemical Properties and Pharmacological Action of the Wood from which it is prepared." By THOMAS R. FRASER, M.D., F.R.S., Professor of Materia Medica in the University of Edinburgh, and JOSEPH TILLIE, M.D. (Edin.). Received March 6, 1893.

Burton,* Cameron,† and other travellers have given accounts of much interest of an arrow-poison used in warfare and in the chase by the Wa Nyika, Wa Kamba, Wa Gyriama, and other tribes of Eastern Equatorial Africa. The poison was stated to be prepared from the wood of the stem and root of a tree, which, however, was not botanically identified.

Several years ago, an opportunity was given to one of us to examine poisoned arrows, and the poison used in smearing them, of the Wa Nyika tribe. While the pharmacological action of this poison was found to have a close resemblance to that of *Strophanthus* seeds, its physical and chemical properties enabled the conclusions to be drawn that the poison was not made from these seeds, but was chiefly composed of an extract prepared from a wood.‡

These conclusions have been confirmed by the examination of further specimens of the Wa Nyika arrow-poison, and of the wood from which it is prepared. The specimens were most kindly sent to one of us, at various times between 1889 and 1892, by the Rev. William Morris, of the Church Missionary Society's East African Mission, and by Mr. Berkeley, the Administrator to the Imperial British East Africa Company at Mombasa.

These gentlemen have also sent the leaves and fruit of the plant, which have enabled us to identify it as an *Acokanthera;* but, as flowers have not yet been obtained, it has not been possible to determine the species.

* 'The Lake Regions of Central Africa,' 1860, vol. 2, p. 305.

† 'Across Africa,' 1885, p. 59.

‡ Fraser, "On *Strophanthus hispidus:* its Natural History, Chemistry, and Pharmacology," 'Edinburgh Roy. Soc. Trans.,' vol. 35, Part IV, 1890, pp. 966–67.

In the present paper we propose to give a brief preliminary description of some of the most important of the results obtained by us in an extended examination of the chemical and pharmacological properties of the arrow-poison, and especially of the wood from which it is prepared, reserving fuller details until the flowers of the plant have been obtained.

We have found that the arrow-poison contains a crystalline glucosidal active principle, which in its chemical properties and pharmacological actions is identical with an active principle present in the wood, thus confirming the statement of the source of the poison.

One early and small supply of the wood did not yield a crystalline principle when the extract was treated by the tannin and oxide of lead process, and the limited supply at our disposal prevented the adoption of the process which, when applied to subsequently received supplies, led to the separation of the active principle in a crystalline form.

This process consists in the preparation of an alcoholic extract of the wood, the treatment of this with water, and the evaporation of the filtered watery solution. Impure crystals appear in the concentrated fluid, and their purification is effected by digestion of a hot alcoholic solution with charcoal, and subsequent recrystallisations from rectified spirit.

Thus obtained, the active principle occurs in the form of colourless thin needle-shaped crystals, which usually group themselves in tufts and rosettes. When crystallised from water it has the form of quadrangular plates.

At a temperature between 55° and 60° F. the crystals are soluble to the extent of about 0·93 per cent. in distilled water; of 0·41 per cent. in absolute alcohol; of 0·45 per cent. in diluted alcohol of sp. gr. 0·838; of 2·4 per cent. in diluted alcohol of sp. gr. 0·920. They are less soluble in acetone, amylic alcohol, and petroleum ether; and are altogether insoluble in ethylic ether and chloroform. Much larger quantities are dissolved by hot than by cold water and alcohol.

Ether, chloroform, and petroleum ether precipitate the active principle in a crystalline form from solutions in strong and dilute alcohol.

A saturated solution in cold water is tasteless and neutral in reaction; and it is obviously affected by very few chemical reagents, including the ordinary reagents for alkaloids. Silver nitrate and mercurous nitrate, however, produce white precipitates. Tannin does not cause any change in saturated cold water solutions, but it throws down a copious white precipitate in cold solutions, prepared by saturating water at the boiling temperature, and this precipitate is soluble in an excess of the reagent and in water.

When to the crystals themselves a little strong sulphuric acid is added, a pink colour is almost immediately developed, which soon darkens to a brick-red, and then slowly fades to pale brown. Dilute sulphuric acid, with moderate heat, changes the colourless crystals rapidly to brick-red, and then gradually chocolate and green colours are developed.

The exact melting point is not easily ascertained. When heated to about 184° C., the crystals suddenly almost disappear, and the soft substance remaining undergoes little further change until a temperature of rather over 200° C. is reached, when the colour becomes brown, and bubbles of gas are liberated.

No nitrogen or inorganic matter is present in the crystals. When they are heated at 100° C. in 2 per cent. sulphuric acid, a brownish amorphous substance is deposited, and the neutralised filtrate causes an abundant reduction in Fehling's solution, showing that the active principle is a glucoside.

Two concordant combustions made for us by Dr. Dobbin, of the Chemical Laboratory of the University, indicate that the probable formula of the substance is $C_{30}H_{52}O_{14}$.

These characters show that this active principle closely resembles, if it be not identical with, a crystalline substance separated by Arnaud,* by a more complicated process than the above, from the wood of a plant obtained in the Somali country; and, although the species has not yet been identified, the plant has, from an examination of the twigs and wood, been placed in the genus *Acokanthera*.†

On testing the pharmacological activity of the crystalline active principle obtained by us from the *Acokanthera* wood, we found that the minimum lethal dose for the frog (*Rana temporaria*) was between 0·00004 and 0·00005 grain per 100 grains of weight of frog. The latter dose always caused death, usually in from three to six hours; the former dose was not lethal. Rabbits died usually in a little over an hour after the subcutaneous administration of from 0·00003 to 0·000035 grain per 100 grains (1/400th to 1/500th grain per pound) of weight of rabbit.

The arrow-poison itself was found to have only one-fourth the lethal power of the crystalline active principle.

In a series of experiments on frogs and rabbits we found certain effects to occur so uniformly that they may be regarded as characteristic of the action of the poison.

In the frog the prominent effects which follow the subcutaneous injection of large lethal doses are:—Slowing and intermittence of respiration; gaping of the mouth, often accompanied with straining

* 'Comptes Rendus,' vol. 106, 1888, p. 1011, and vol. 107, 1889, p. 1162.

† *Ibid.*, vol. 107, 1889, p. 1162, and 'Bulletin Gén. de Thérap.,' vol. 117, 1889, p. 107.

movements like those of vomiting; fibrillary twitching of muscles, especially at the seat of injection; impairment of motor power and of co-ordination; disappearance of the cardiac impact; cessation of respiration; and gradual enfeeblement and loss of reflex and voluntary movement.

On opening the thorax, the heart is found motionless, the ventricle in extreme systole, the auricles distended with blood, and the whole heart inexcitable to mechanical or electric stimulation. When, however, the precise minimum lethal dose has been administered, the heart is found to have been arrested in extreme diastole, and it responds to stimulation. Immediately after death, stimulation of a motor nerve causes muscular contraction; but, soon thereafter, the muscles cease to respond to stimulation of the nerves or to direct irritation, and become acid in reaction and rigid.

In the rabbit, after the subcutaneous administration of a minimum lethal dose, the most important phenomena are gradual impairment and failure of the heart's action, of respiration, and of motor power. Just before death the cardiac pulsations become slow and extremely feeble, but the rate is estimated with difficulty by palpation of the thorax on account of frequent muscular twitchings. The respiration is rendered slow, irregular, and shallow. Inspiratory difficulty occasionally becomes so great that death from asphyxia seems impending even when the cardiac pulsations and general motor power appear good. Motor power is usually so much reduced before death that the animal lies prostrate; and only a few feeble movements of the body indicate the arrest of the heart. When the dose is large, or when the poison acts with unusual rapidity, the heart is paralysed before the general motor depression has set in, and sharp convulsive movements follow the arrest of the circulation. It is sometimes difficult to say whether the cardiac or the respiratory movements cease first. Usually, respiration is distinctly continued for a brief period after the heart can no longer be felt to pulsate, and on *post-mortem* examination, the bright red colour of the left auricle and the pulmonary veins contrasts strongly with the dark colour of the right auricle. Sometimes cardiac movements occur after the respiration has finally ceased, but immediate *post-mortem* examination reveals that the pulsations are mere irregular movements, altogether insufficient to sustain life or to indicate that the arrest of respiration was the cause of death. The left ventricle is usually found contracted and nearly empty, and the right ventricle and the auricles filled with blood. Most frequently the heart is motionless, and does not respond to mechanical or electrical stimulation, but it sometimes shows spontaneous quivering movements, and, for a very brief period, may respond to stimulation. The lungs are of a light pink colour. After death, the motor nerves soon lose all influence over

the muscles, and, in a very brief period thereafter, the muscles become inexcitable, acid in reaction, and rigid.

On analysing the action of the active principle we have found that, in the frog, the slowing, irregularity, and cessation of respiration, and the gaping movements of the mouth are not necessarily primary actions, but may be secondary to the arrest of the circulation, because control frogs, whose circulation has been mechanically arrested, exhibit these phenomena within a similar period of time. In rabbits, artificial respiration does not prevent death from cardiac failure; but the impairment of respiration probably contributes in them to the fatal result in the case of doses bordering upon the minimum lethal.

The fibrillary muscular twitchings which occur in rabbits as well as in frogs are due to a primary action upon the endings of motor nerves.

The disappearance of reflex and voluntary movements after the administration of small lethal doses is due to paralysis of the nerve centres, and not to a peripheral action, for when one part of the body is protected, reflex and voluntary movements cease in the protected and unprotected parts at the same time. This central paralysis, however, is almost entirely due to the failure of the circulation, and resembles the paralysis in unpoisoned control frogs whose circulation is arrested. When large doses of the poison are administered subcutaneously to frogs, the depression of reflexes is partly due to peripheral causes, because, when one part is protected, that part exhibits more rapid and vigorous reflexes than the unprotected parts. This difference is largely due to a paralysing action on the muscles. It may, however, be partly caused by depression of sensibility, for when the action is limited to one part, stimulation of the skin in the poisoned area fails, after a time, to cause reflexes in the unpoisoned parts, although stimulation of a poisoned nerve trunk still excites reflex movements. The action of large doses upon the sensory nerves is well shown by applying 1/100th of a grain in solution to the cornea of the rabbit, when anæsthesia, lasting for several hours, along with some contraction of the pupil, is produced.

The motor nerves retain their influence upon the muscles until the latter show distinct signs of poisoning; but the muscles still react to strong, although not to moderate, electrical stimulation after stimulation of their motor nerves is no longer able to excite contractions.

The action on the heart is very pronounced. When a large dose is injected subcutaneously in the frog, or applied directly to the heart, the pulsations become slow owing to a great increase in the duration of the systole. Unequal contraction and relaxation of parts of the ventricular wall occur, the diastolic expansion becomes less and less, and, within twenty minutes after poisoning, the ventricle is arrested

in extreme and permanent systole. The auricles contract for a short time longer, but cannot empty themselves, and become arrested in a dilated state. The heart no longer responds to stimulation, and the muscle of the ventricle quickly acquires an acid reaction. After arrest of the heart, respiration may continue irregularly for so long as an hour, and for a time the frog can jump about actively.

The action of small doses upon the heart is, in several respects, essentially different from that of large doses. Several hours after the administration of the precise minimum lethal dose, the cardiac pulsations become very slow. The slowing, however, is not due to a lengthening of the systole, but to a great prolongation of the diastole, and of the succeeding pause in the heart's action. Gradually, periods of standstill occur in extreme diastole, and, when the heart spontaneously resumes beating, one or more auricular contractions precede those of the ventricle. The systolic contraction is extremely powerful. The condition of diastolic arrest often lasts many minutes at a time, and finally spontaneous pulsations cease. At this stage, the dilated heart responds, by one or more contractions, to any form of stimulation, but, if the stimulation be frequently repeated, the relaxation after each contraction becomes less and less, and the ventricle slowly passes into moderate, but permanent, systole. During these events, the inhibitory function of the vagus is not only retained, but increased. The diastolic arrest of the heart is not dependent upon "inhibition," however, for the condition is neither removed nor prevented by the administration of atropine. The accelerator action of the vagus is retained. The diastolic arrest is apparently due, therefore, to a direct action of the poison upon the motor ganglia and muscle of the heart.

The action upon the blood-vessels was found to be very slight. One part of the crystalline active principle in 10,000 parts of normal saline solution (0·75 per cent.) produced, when circulated through the vessels of a pithed frog, about the same effect as the pure saline solution, whereas 1 part of Merck's purest digitalin (soluble in water) in 50,000 parts of normal saline solution produced an extreme and rapid reduction in the calibre of the vessels. This difference in action upon the vessels is much accentuated by the fact that the lethal power of the digitalin in frogs was found to be only about 1/50th of that of the active principle of the *Acokanthera* wood.

In blood pressure experiments upon rabbits, the repeated administration of small non-lethal doses by injection into the jugular vein produced a remarkable slowing of the pulse, the vertical height of each pulse curve indicating at the same time a great increase in the force of the ventricular contraction. The blood pressure was usually found not to be increased, and, when increased, was evidently not the cause of the slow pulse. When rise of blood pressure from asphyxia

was guarded against by carrying on artificial respiration, the pressure was little affected, except when a marked fall occurred before death. The inhibitory action of the vagus was found to be retained, and the nerve proved to be intimately concerned in the early slow pulse, because the division of the vagi or the administration of atropine produced an immediate change in the tracing, the pulse becoming rapid and the movements relatively small. The further administration of the active principle restored to only some extent the original character of the tracing. When large doses were administered, the original slow pulse quickly became rapid and irregular, the blood pressure rose somewhat, and the respiration became disordered. The pressure then rapidly fell, and the cardiac pulsations became slow, intermittent, and feeble, and finally ceased before the pressure was at zero.

The action upon the circulatory, muscular, and nervous systems, therefore, closely resembles, if it be not identical with, that of strophanthin.

*Note.*

In 1880, an arrow-poison used by the Wa Nyika and Wa Kamba tribes was examined chemically by Gerrard,* and a non-crystalline substance, giving the reaction of a glucoside, was separated, and was found by Ringer* to be a powerful muscle-poison, which caused death by arresting the heart in systole. In 1887, Laborde† examined some features of the physiological action of a Wa Kamba arrow-poison, obtained from a missionary, M. A. Le Roy, and stated by him to be composed of parts of eight plants. Laborde found that the poison caused death by arresting the respiration and heart, and he came to the conclusion that the primary and predominant action was exercised upon the cardio-respiratory centres in the medulla.

In 1888, MM. Langlois and Varigny‡ examined the action of poisoned arrows obtained from the Somali country, and found that the poison caused arrest of respiration and of the heart, which they attributed to paralysis of the medullary centres.

In the same year, MM. Gley et Rondeau,§ and also M. Gley|| separately, examined some points in the action of ouabaïn, the active principle separated by Arnaud from wood believed to be the source of the Somali arrow-poison, and concluded that the effects produced were due essentially to an action upon the medullary centres. Dr. Sailer,¶ in 1891, after an extended examination of the actions of

* 'Pharm. Journal and Trans.,' 1880–81, p. 835.

† 'Comptes Rend. de la Soc. de Biol.,' 1887, vol. 4, pp. 52, 370.

‡ *Ibid.*, 1888, vol. 5, p. 419.

§ *Ibid.*, p. 421.

|| 'Comptes Rendus,' 1888, vol. 107, p. 348.

¶ 'Therapeutic Gazette,' 1891, vol. 15, pp. 727, 814.

ouabaïn, arrived at conclusions which are not in accordance with those of the French observers, viz.:—that the cardio-respiratory centres in the medulla are not primarily affected, that the lethal action of the poison is exercised directly upon the heart, and that the asphyxia is a secondary phenomenon.

The Society then adjourned over the Easter Recess to Thursday, April 20.

*Presents, March* 23, 1893.

Transactions.

Baltimore:—Johns Hopkins University. Circular. Vol. XII. No. 103. 4to. *Baltimore* 1893; Register 1891–92. 8vo. *Baltimore* 1892. With a series of Dissertations and Theses. The University.

Boston:—Boston Society of Natural History. Memoirs. Vol. IV. No. 10. 4to. *Boston* 1892; Proceedings. Vol. XXV. Parts 3—4. 8vo. *Boston* 1892. The Society.

Cambridge, Mass.:—Harvard College. Annual Reports, 1891–92. 8vo. *Cambridge* 1893. The College.

Museum of Comparative Zoölogy, Harvard College. Bulletin. Vol. XXIII. No. 6. Vol. XXIV. Nos. 1—2. 8vo. *Cambridge* 1893. The Museum.

Copenhagen:—K. Danske Videnskabernes Selskab. Oversigt. 1892. No. 2. 8vo. *Kjöbenhavn;* Skrifter (Naturv. og Math.). Bd. VI. No. 3. Bd. VII. No. 6. 4to. *Kjöbenhavn* 1892. The Society.

Frankfort-on-Oder:—Naturwissenschaftlicher Verein. Helios. Jahrg. 10. No. 9. 8vo. *Frankfurt a.O.* 1892; Societatum Litteræ. Jahrg. 6. Nos. 11—12. 8vo. *Frankfurt a.O.* 1892. The Society.

Genoa:—Società Ligustica di Scienze Naturali e Geografiche. Atti. Vol. IV. No. 1. 8vo. *Genova* 1893. The Society.

Kharkoff:—Section Médicale de la Société des Sciences Expérimentales. Travaux. 1892. 8vo. *Kharkoff* 1892. The Society.

Klausenburg:—Erdélyi Muzeum. Értesitö. Évfolyam XVII. 8vo. *Kolozsv'art* 1892–93. The Museum.

Königsberg:—Physikalisch-Oekonomische Gesellschaft. Führer durch die Geologischen Sammlungen des Provinzialmuseums. 8vo. *Königsberg in Pr.* 1892. The Society.

Lille:—Université. Travaux et Mémoires. Tome II. Nos. 7—9. 8vo. *Lille* 1892. The University.