

AN INVESTIGATION INTO CASES OF SUSPECTED POISONING IN AFRICANS IN NORTHERN RHODESIA

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This investigation was undertaken following a letter dated 19 November 1959, in which Dr. M. H. Webster, at that time Director of Medical Services of the Federation of Rhodesia and Nyasaland, sought my advice in connection with serious mortality from a mysterious disease affecting a certain tribe of Africans in Northern Rhodesia.

History

Dr. Webster supplied me with full details of all aspects of the disease. I collected further valuable information during the course of a meeting he called at Lusaka. It was attended by various officers of his Department and by a veterinary officer, a botanist, and an officer of the Department of Fisheries; as well as by an officer of the Criminal Investigation Department. I also obtained information in the course of my own investigation in the affected area, during which I was accompanied by Dr. Webster, Dr. E. Tauber (specialist surgeon at Lusaka), Drs. A. Haworth and A. W. Iljon (medical officers of the Department of Health, Lusaka), Mr. Elvidge (medical inspector), and officers of the Northern Rhodesian Police and Criminal Investigation Department.

The construction of the Kariba Dam in the Zambesi River necessitated the removal of some 50,000 Africans from the basin of the dam to re-settlement areas. The move was completed in October 1958, and the mysterious disease and deaths started in the beginning of September 1959. The following were significant features of the disease:

Some villages were harder hit than others.

There were strong family connections between the consecutive cases of the disease.

According to information supplied by Dr. Webster, 'the trouble was limited to a small group of villages containing some 500 people and fairly sharply localized in an area 2-3 miles in diameter in the angle formed by the confluence of the Lusita with the Zambesi River'.

Mortality was very high (about 80-90%) and most patients died within 24 hours after the onset of symptoms. Young children usually died within 6 hours after being taken ill. Up to the time of my visit to Northern Rhodesia (December 1959) some 80 victims of the disease had died.

The African tribe attacked by the mysterious disease was the most 'uncivilized' of the tribes moved to the new settlement area. This tribe was also the one that was moved the longest distance away from their original homeland. Members of this tribe took very reluctantly to eating the European type of food (maize, beans, etc.) and lived chiefly on the fruits, roots and tubers of wild plants.

Although there was free movement and close contact between the inhabitants of the affected villages and other parts of the re-settlement area, no cases appeared among members of the other tribes.

Only adult females and children of both sexes under 16 years of age were affected, males above 16 years of age

not developing the disease. This phenomenon at once directed my attention to the fact that boys under 16 years of age and all females had their meals together, while males above 16 years had their meals separately. While the males were occupied in the building of houses and the tilling of lands in the re-settlement area, the females and children under 16 years of age went out into the bush (forest) to collect food, which consisted almost solely of the fruits, roots and tubers of wild plants.

At the time the disease broke out, the affected area was afflicted by a very severe drought, and one effect of this was that the above-ground portions of the wild plants had been severely damaged, with the result that it was very difficult for the Africans to identify the plants, especially those species that resembled the species they had been accustomed to eating in their abandoned homeland. This often led to confusion, with the result that poisonous plants were mistaken for edible species, with fatal results.

Symptoms

When Europeans conduct investigations into diseases in African territories, they operate under great disadvantages because they are seriously hampered in their efforts to obtain reliable information. This is due chiefly to witchcraft and to various African customs and beliefs, which vary from race to race and from tribe to tribe. Africans very reluctantly give permission for specimens to be taken from their people or from food or other materials in their huts or on their lands. They are also most reluctant to give permission for the conducting of autopsies and the removal of specimens of organs. In spite of these difficulties all of us who were concerned in the investigation into the cause(s) of the disaster that had befallen this African tribe received the friendly cooperation of a number of the Africans; the African police especially were of great assistance to us. This, I am sure, was due to the fact that they realized that we were genuinely interested in helping them as much as we possibly could. However, if we had been permitted to take more specimens from victims of the disease and to conduct more autopsies, our difficult task would have been much easier, the results of our investigation more reliable, and our conclusions more definite.

The following are the symptoms described by Dr. M. H. Webster, Dr. A. Park, Dr. E. Tauber, Dr. K. G. Gadd, Dr. A. W. Iljon and Dr. A. Haworth.

Peracute cases. In a few cases, children who had apparently been well when last seen, were found dead a few hours later, in some cases under trees and bushes.

Acute cases. Young children usually died within 4-6 hours of the onset of symptoms, while older children and adults lived up to 24 hours or longer. Children who had gone to bed apparently in good health would wake up in the early hours of the morning, complaining of thirst. They were restless and the drinking of water appeared to

aggravate the symptoms. The following symptoms were in evidence: vomiting (in some cases); precordial discomfort; loose stools; very fast and thready pulse; pulmonary oedema; apprehension; restlessness; dizziness; headache; abdominal irritability towards the end; hypertonicity of the limbs, which were constantly moved; enlarged liver; jaundice (in some cases); pupils in some cases normal, in some dilated, and in some constricted; towards the end there were signs of pronounced renal irritation (marked albuminuria, scanty urine, and red cells and granular and cellular casts in the urine); prostration; delirium; sometimes profuse sweating, coma, and shock. In most cases fever was absent, while a few cases showed minor degrees of fever. Dr. Gadd established a pronounced hypoglycaemia, the liver being negative for glycogen. This appears quite conceivable owing to the very severe liver damage.

Treatment with various drugs (sulphonamides, tetracyclines, atropine, alcohol) had no effect.

Postmortem Appearances

Dr. K. G. Gadd, Director of the Public Health Laboratories, Lusaka, conducted 12 autopsies and found the following: All cases showed very severe damage of the liver, kidneys, spleen, and heart; pronounced oedema of the lungs; sloughing of the mucosa of the small intestine, right into the deepest layers; contents of the large bowel softish.

Histology (Dr. K. G. Gadd)

Liver. Marked degree of necrosis of the centre of the lobules, with fatty degeneration.

Kidneys. Very marked fatty degeneration and necrosis of the tubules (nephrosis rather than nephritis).

Heart. All stages of degenerative changes.

Spleen. Massive necrosis.

Submandibular gland. Degenerative changes with marked desquamation in the salivary duct.

Adrenals. Generally normal.

Cerebrospinal fluid. Normal.

Cerebral cortex. Mainly oedema with no exudative response. Neurone changes are early degenerative.

Pancreas. Gross degeneration, with no nuclear staining.

Dr. Gadd kindly supplied me with specimens of the organs of 3 of the deceased victims. I had hoped that the results of our histological examination might give us an indication of a possible plant poison. These specimens I submitted to colleagues at the Onderstepoort Research Laboratories, where they have had extensive experience of the pathology of many plant and other poisons in animals. For their valuable assistance I am greatly indebted to Prof. T. Adelaar, Department of Toxicology, to Prof. A. de Boom and Dr. R. C. Tustin, of the Department of Pathology, and to Dr. R. Ortlepp and other colleagues. They reported that all 3 cases showed severe necrobiosis of the liver, very severe nephrosis, and degenerative changes in the myocardium. All 3 also showed degeneration of the brain neurones. One case showed microfilariasis. These results confirmed Dr. Gadd's findings and also my view, expressed in my letter of 3 December 1960 to Dr. M. H. Webster, namely, that all the information submitted to me was characteristic of severe intoxication.

THE AUTHOR'S INVESTIGATION

On 11 Dec. 1959 Drs. Webster, Tauber, Iljon, Haworth and I visited the affected area. There we met officers of the N. Rhodesian Police and the Criminal Investigation Department, and Mr. Elvidge, medical inspector. Also here I found evidence of the extreme thoroughness with which the officers of each Department concerned had conducted their investigations. The CID and the Police Department investigated the possibility of criminal poisoning. In spite of the most searching and intensive investigation, they failed to find any clues. Through the kind efforts of these two Departments, I obtained specimens of about 40 plants which the tribe concerned used as remedies or relishes. Unfortunately most of these consisted of roots, leaves and branches which were unidentifiable.

Drinking water. Chemical analysis and bacteriological examination of the drinking water supplied at various points revealed nothing harmful to health, and there were no poisonous algae present. As reports had reached Dr. Webster that the toxic South African alga *Polycystis toxica* Kützing (= *P. aeruginosa* Kützing = *Microcystis toxica* Stephens) had been found on the Kariba Dam, I was requested to visit the dam. An intensive search was made for this very toxic alga, which has been killing thousands of stock, fish and birds in South Africa, but no trace of it could be found. Unfortunately the Kariba Dam is infested with the plant *Salvinia auriculata*, which is

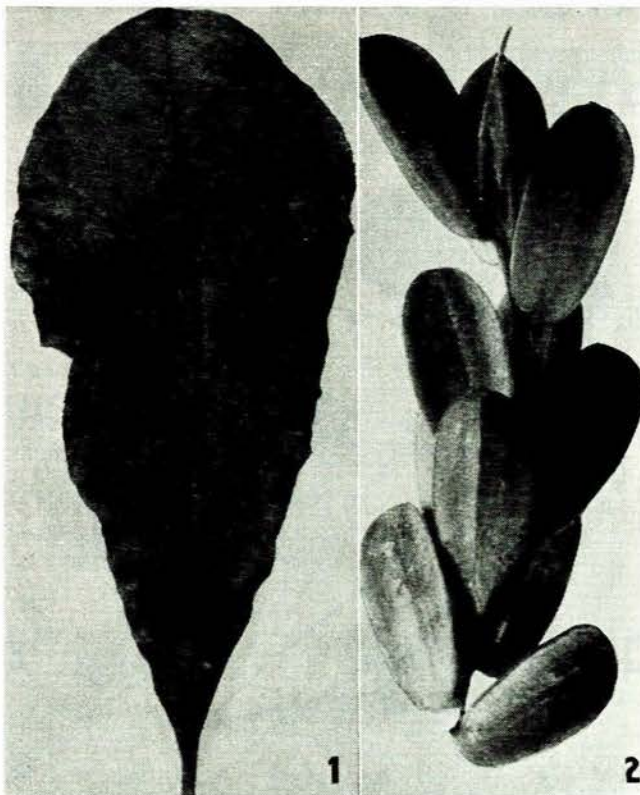


Fig. 1. Leaf of *Dioscorea quartiniana* A. Rich.
Fig. 2. Fruit of *Dioscorea quartiniana* A. Rich.

indigenous to South and Central America.

Food. The Africans in the re-settlement area eat similar foods. Maize, beans and kaffircorn are either produced by themselves or are bought at the various stores. Some of them also eat either dried fish or fresh fish caught in the rivers. Cassava is eaten to a limited extent. However, the afflicted tribe being the most 'uncivilized' of all the tribes, they ate very little or none of the foods (kaffircorn, beans, maize, etc.) that were obtainable at the local stores. Various kinds of plants are eaten as relishes, either in their raw state, or after having been cooked or boiled for a few hours.

Collection of Specimens of African Medicinal Herbs and Wild Food Plants

At my request, European and African officers of the Police Department and mothers and relatives of a number of the victims of the mysterious disease accompanied me on my field investigations. The mothers and relatives pointed out to me what wild fruits, roots and tubers they were and had been eating. I was informed that the tribe concerned were particularly fond of a tuber *Dioscorea quartiniana* A. Rich (Figs. 1 - 3), which resembled another tuber, *Dioscorea schimperiana* Hochstetter ex Kunth (Figs. 4 and 5), which constituted one of their staple foods in their previous homeland.

As a result of the severe drought that was prevailing at the time in the new settlement, the runners of these two plants were leafless, and even dead. Consequently, it was very difficult for the Africans to distinguish between

them. As I knew that several species of *Dioscorea* were poisonous, I decided to conduct biological tests with these two species and with some other plants that were being

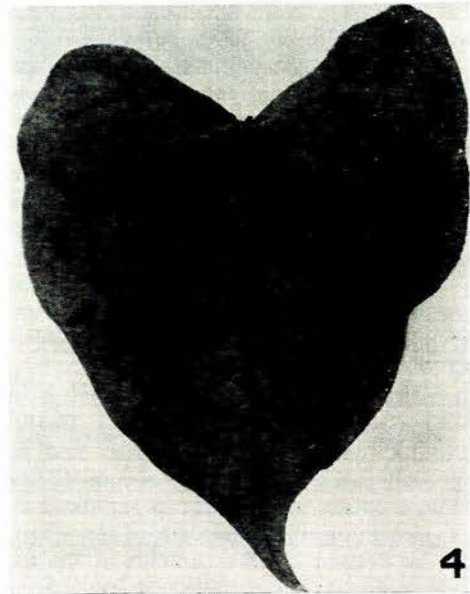


Fig. 4. Leaf of *Dioscorea schimperiana* Hochstetter ex Kunth.

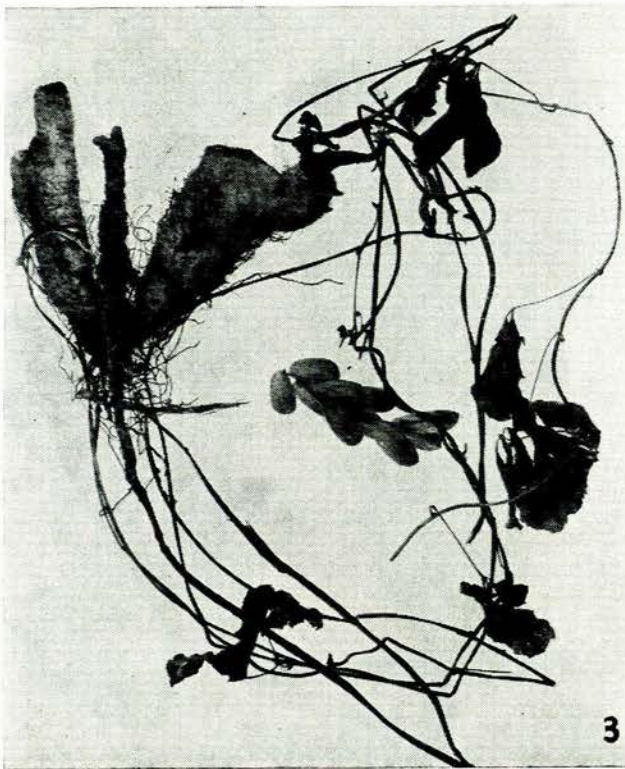


Fig. 3. Tubers and runners with leaves and fruit of *Dioscorea quartiniana* A. Rich.

eaten by the African tribes. As stated above, the other African tribes included maize, kaffircorn, beans, cassava and fish in their diets, while the afflicted tribe lived chiefly on wild plants.

On the reaped mealie and kaffircorn lands, I found two poisonous plants that on several occasions had caused severe losses in cattle and sheep in South Africa. They were *Epaltes alata* Steetz. and *Acalypha indica* L. I was informed that more than a thousand sheep and goats had died in the area and environment where the mysterious

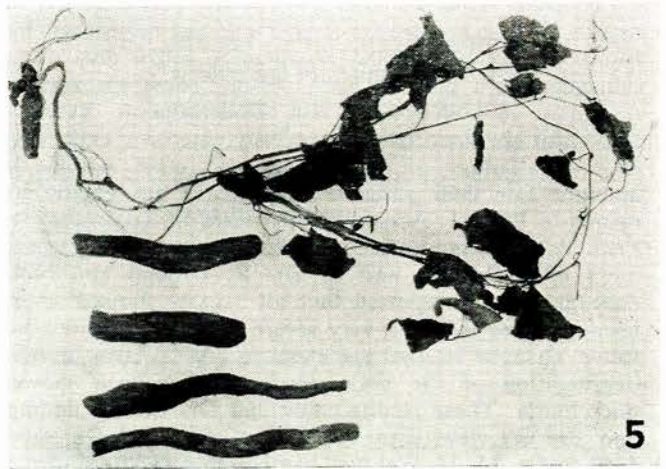


Fig. 5. Runners with leaves and rhizomes of *Dioscorea schimperiana* Hochstetter ex Kunth.

disease had claimed its victims. As the grazing was very scanty and dry it is possible that the animals had eaten these two poisonous plants. *Acalypha indica* L. contains large quantities of hydrocyanic acid and may cause sudden death when eaten. This plant somewhat resembles several species of *Amaranthus* (pigweed, 'marôgo'), which is a well-known and popular relish among Africans, and confusion of the two plants may be the cause of poisoning and death. I should add that *Amaranthus*, especially when growing on lands treated with nitrogenous fertilizers, is dangerous to young children, for it contains large amounts of nitrate, which constitutes a grave danger to very young children when present in appreciable amounts in drinking water and food plants.²² Nitrates and nitrites are known to cause methaemoglobinemia.

Among the plant specimens handed to me was the Mgongo nut, which I recognized as the nut I had collected in the Eastern Caprivi Strip in 1953 while on an investigation into endemic goitre, which we found to be caused by iodine deficiency.⁸ It is the fruit of the tree *Ricinodendron rautanenii* Schinz., and is edible.⁸

BIOLOGICAL TESTS

I conducted biological tests on young rabbits with plants collected in the affected area. The plant material was administered by stomach tube in quantities varying from 1.0 to 10.0 G per kg. body weight daily for 4 days, if the animals did not die before this period expired:

1. *Cordyla africana* Lour. ('Sozwe' or wild mango). Fresh immature and mature fruits.
The animals suffered no harmful effects whatever.
Tests for hydrocyanic acid were negative.
The fresh mature fruit is edible, and is rich in ascorbic acid.⁵
2. *Dioscorea schimperiana* Hochstetter ex Kunth. Fresh tubers. The tubers proved to be non-toxic.
3. *Dioscorea quartiniana* A. Rich. Fresh tubers.
The LD₅₀ of the tubers for rabbits was 5.0 G/kg. body weight.
No hydrocyanic acid was detectable in the tubers.
Cooking the poisonous tuber for half-an-hour destroyed the active principle and rendered the tuber edible.

(a) *Symptoms of Dioscorea quartiniana poisoning in the rabbits.* The following symptoms appeared within a few hours after dosing: progressive listlessness, tachycardia, accelerated respiration, intermittent restlessness and diarrhoea. Death, preceded by coma and terminal convulsions, occurred within 24-48 hours after the initial dose.

(b) *Autopsy findings.* Severe congestion and oedema of the lungs; enlarged spleen; varying degrees of acute gastroenteritis; soft and friable liver.

(c) *Histology.* I am indebted to Dr. R. C. Tustin, of the Department of Pathology, Veterinary Research Institute, Onderstepoort, for the histological examination of specimens of organs of the experimental rabbits, and the following report: liver, degenerative changes; kidney, moderate nephrosis; lungs, severe congestion; spleen, old

cells undergoing karyorrhexis; myocard, mild degeneration of odd segments of muscle fibres.

(d) *Isolation of the toxic principle(s) of Dioscorea quartiniana.* Dr. J. R. Nunn, Professor of Organic Chemistry, Rhodes University, Grahamstown, did not succeed in isolating any toxic material from *Dioscorea quartiniana*. He did, however, isolate a crystalline glycoside that did not appear to be toxic. Professor Nunn is continuing his investigations.

4. *Acacia albida* Del. ('Ana tree' of South West Africa and Transvaal). Seeds.

This tree occurs almost throughout Africa and the pods are eaten by stock, antelope, camels and elephants. (For further information see Watt and Breyer-Brandwyk.⁵)

As I was told that the seed of this tree was eaten by some of the Africans, I thought it advisable to submit it to a toxicological test.

Four rabbits (each weighing 2.0 kg.) received (A) 40 G of the mature seed in 2 days, (B) 80 G in 4 days, (C) 80 G in 2 days, and (D) 45 G in 2 days respectively. A died within 24 hours, B within 7 hours, C within 40 hours, and D within 60 hours after the first dose.

(a) *Symptoms of poisoning with the mature seed of Acacia albida.* The animals exhibited listlessness, laboured respiration, tachycardia, anorexia, and diarrhoea.

(b) *Autopsy findings.* Congestion of the lungs, soft and friable liver very light in colour, large petechiae in the gastric mucosa, and hyperaemia of the intestinal mucosa.

(c) *Histology (Dr. R. C. Tustin, Veterinary Research Institute, Onderstepoort):* Liver: 'Cloudy swelling; mild round-cell infiltration into portal tracts; fairly large foci of necrosis situated irregularly in the lobuli and manifested by an eosinophilic cytoplasm of hepatic cells; pyknotic, karyolytic or karyorrhectic nuclei; congestion; mild fatty changes and cloudy swelling of cells not undergoing necrosis.' Spleen, nothing specific. Kidney, severe cloudy swelling. Heart, hyperaemia, few petechiae. Lung, partial collapse, hyperaemia, some oedema. Stomach, petechial haemorrhages, mild focal infiltration (diffuse) of neutrophils. The severest damage to the organs, especially the liver, was seen in the rabbits that had lived longest.

(d) Tests for *hydrocyanic acid* in the mature seed yielded negative results. This is in contrast to my previous experience with seed collected in South West Africa and which showed quite appreciable amounts of this substance. As stated above, stock and other animals eat the pods. The fact that they do this with apparent impunity is possibly because the poisonous principle in the mature seed is inactivated or counteracted by the large amount of tannic acid in the shells of the pods. The pods may contain up to 14.3% of tannic acid.⁵ Apparently Africans also eat the mature seed. These seeds are very hard and are cooked or boiled in water for a long time, with the result that the poisonous principle is destroyed.

REVIEW OF LITERATURE ON SPECIES OF 'DIOSCOREA' *Toxic Principles and other Chemical Constituents of the Tubers of Species of Dioscorea*

The following summary has been compiled from information supplied by Wehmer⁸ (pp. 167-168), Watt and Breyer-

Brandwyk⁶ (pp. 383-387), and Dr. L. E. Codd, Chief of the Botanical Research Institute, Pretoria. It comprises the name of the species, their country or countries of origin, and their chemical composition.

1. *D. abyssinica* Hochst.⁵ Central Africa. Tuber edible.
2. *D. oculatea* L.⁵ S.E. Asia. Tuber cultivated (yam)—starch, sugar, fat.
3. *D. alata* L.⁵ (var. *purpurea* = *D. purpurea* Roxb.) Tropical America, W. Africa, S.E. Asia. Tuber edible boiled or roasted (yam)—starch, saccharose, fructose. Tuber also contains trace of toxic alkaloid and is applied to sores. Leaf juice is applied to scorpion stings.
4. *D. batatas* DeNE³ (+ *D. divaricata* Blinc.) Philippines, China, Japan. Cultivated in Brazil. Important food (yam and arrowroot). Starch, sugar, fat, mucin.
5. *D. buchani* Benth.⁵ (?) N. Rhodesia, Tanganyika, Nyasaland. Steam from boiling leaf inhaled for anaemia and oedema.
6. *D. bulbifera* L.⁵ Tropical Asia and Java. Cultivated in East and Tropical Africa and Tropical America. Aerial tubers large and edible. Subterranean tubers small and acrid tasting, said to be poisonous but eaten after steeping in water and ash. Tubers contain starch, sugar and protein, *diosgenin*, tannic acid, organic acids, (a poisonous 'glycoside' in some countries).
7. *D. cirrhosa* Lour.⁵ E. Asia. Tuber cultivated (yam)—starch, sugar, fat.
8. *D. cotinifolia* Kunth.⁵ E. Cape Province, Natal, Transvaal, Mozambique. Xhosa use root for binding asagai. Contains tannin.
9. *D. diversifolia* Kunth.⁵ Zululand, E. Cape Province, Natal. Zulus use tuber for hysterical fits.
10. *D. dregeana* Dur. and Schinz.⁵ (var. *Hutchinsonii* Burkil.) Eastern parts of S. Africa, E. Transvaal. Tuber apparently poisonous, but edible if soaked in water for a few days; raw it causes paralysis of legs and symptoms like drunkenness. Africans use tuber as soporific and aqueous extract of tuber as lotion for wounds and sores in man and animals and for local pain.
11. *D. dumetorum* Pax.⁵ Tropical and subtropical Africa, tropical parts of the East (Java). Used for schistosomiasis in Tanganyika, and tuber as monkey poison by Zulus. Tuber produces symptoms like drunkenness, but is edible after soaking in water several days. Africans have bred less poisonous and less bitter strains. The wild plant contains *dioscorine* and also *dihydrodioscorine* (a convulsive poison, with LD₅₀ of 65 mg./kg. when injected intraperitoneally into mice).
12. *D. elephantipes* Engl.⁵ (= *D. testudinaria* Lubbock = *Testudinaria elephantipes* Lindl.), elephant's foot, or Hottentot bread. From Clanwilliam to Albany district, S. Africa. Used as food—starch, sago; alkaloids, tannin, organic acids; *diosgenin*.
13. *D. hemicypta* Burkill.⁵ (= *Testudinaria glauca* Marl.) Southern Cape Province. Tuber contains an 'alkaloid' and tests for haemolysis have been positive.
14. *D. hirsuta* Bl.⁵ S.E. Asia. Tuber is a fish and arrow poison, but is edible when cooked. Contains *dioscorine*, a toxic alkaloid.
15. *D. japonica* Thbg.³ E. Asia. Tuber rich in sugar, fat and mucin.
16. *D. macabiha* Jum. et Perr.³ Madagascar. Tuber poisonous—enzymes (invertase, amylase), starch, sugar (no glycosides or alkaloids).
17. *D. oppositifolia* L.³ E. Asia. Cultivated as food (yam)—starch, fat, sugar.
18. *D. pentaphylla* L.³ S.E. Asia. Tuber contains trace of poisonous alkaloid.
19. *D. retusa* Mast.⁵ Eastern S. Africa. Tests for haemolysis and for presence of alkaloids, tannin and organic acids have been negative.
20. *D. rupicola* Kunth.⁵ E. Cape Province and Natal. Tuber used as fish poison—*dioscorine*—but said to be eaten when boiled by the Zulu in times of famine.
21. *D. sansibarensis* Pax.⁵ Tropical E. Africa. Tuber has been used in Africa as fish poison and homicidally, but is said to be used as food in Tanganyika and in India. Bantu used green parts as 'spinach'. Plant said to contain '*dioscorin*' and traces of a toxic alkaloid.³ Tuber contains saponin Saponisides.
22. *D. sativa* L.³ E. Asia. Tuber contains starch.
23. *D. spiculata* Bl.³ (placed by Kunth¹⁰ as synonym for *D. alata* L.). E. Asia. Tuber contains starch and traces of a poisonous 'alkaloid' (see no. 3).
24. *D. sylvatica* Ecklon⁵ (= *Testudinaria sylvatica* Kunth.) E. Cape Province, E. Transvaal, E. and S. Rhodesia. The Zulu make lotion from tuber for udder in mastitis and for douche in infections of uterus in the cow.
25. *D. testudinaria* Lubbock⁵ (probably synonym for *D. elephantipes* Engl.) S. Africa, Mexico, India. Tests for haemolysis and for presence of organic acids and phenols have been positive. Mexican- and Indian-grown tuber yielded 0.5% *diosgenin* (dry weight basis) (see no. 12).
26. *D. tokoro* Mak.³ E. Asia. Tubers used as fish poison¹⁷—contain 2 saponin-like substances *dioscin* (the structure of its aglycone, *diosgenin*, has been determined by Marker et al.) and *dioscorina sapotoxin*.
27. *D. triphylla* L.³ var. *reticulata* Prain and Burkill (= *D. hispida* Dennst.) S.E. Asia. Dried tuber contains 0.21% *dioscorine* (C₁₃H₁₇O₂N).
28. *D. villosa* L.³ (= *D. paniculata* Michx.) N. America from Canada to Mexico. Tuber used for various diseases—starch, saponins, and a resin-like substance '*dioscorin*'.

Various species of *Dioscorea* are known to be poisonous.^{23,24}

Pinder²¹ reports that Boomsma first isolated *dioscorine* (C₁₃H₁₉O₂N) in 1894 from the tubers of *Dioscorea hirsuta* Bl. and, later, in 1937 Leyva and Gutierrez isolated this alkaloid from the tubers of *D. hispida* Dennst. Pinder²¹ goes on to describe the isolation of what he believed to be *dioscorine* from *D. hispida* in his own laboratory at Oxford. Holmes,¹ Fodor² and Jones and Pinder²² discuss the method of extraction and the chemical constitution of *dioscorine*. Jones and

Pinder²² concluded that 2-oxotropane is a degradation product of *dioscorine* and described the formula of this alkaloid.

Van Itallie and Bylsma⁸ describe the following chemical tests for *dioscorine*:

1. A solution of this alkaloid in sulphuric acid turns yellow when a small amount of iodic acid is added to it. From the edge, the yellow colour changes slowly to reddish-violet, which in turn changes to bluish-violet.
2. When a drop of a diluted solution of sodium nitroprusside and a few drops of sodium hydroxide are mixed with *dioscorine*, a reddish-violet colour appears after a short while.
3. If *dioscorine* is heated with sulphuric acid on a water-bath, a reddish-violet colour appears slowly.

Holmes¹ writes: '*Dioscorine* gives a diagnostic colour reaction with potassium iodate and sulphuric acid (188). The brownish-yellow colour, first formed, slowly changes to a bluish-violet'.

Haas and Hill⁴ state that the mucilage present in the roots of *Dioscorea japonica* Thbg. in many of its characteristics resembles mucin obtained from animal sources.

Wall et al.¹⁵ describe the isolation of two new isomeric 12-ketonic sapogenins, *gentrogenin* and *correllogenin* from the tubers of *Dioscorea spiculiflora*.

Meer and Jannke¹⁶ isolated palmitic, stearic, oleic and linoleic acids, as well as a wax, unsaturated hydrocarbons, and a yellow pigmentary material, a β -sitosterol glucoside, from the roots and tubers of *Dioscorea macrostachya* Benth. The material was obtained from Honduras.

Canham and Warren⁷ isolated '*dioscin*' and *yamonin* from *Testudinaria sylvatica* Kunth. (= *Dioscorea sylvatica* Ecklon.) and showed them to be isomeric glycosides of *diosgenin* and *yamogenin* respectively with two molecules of glucose and one molecule of rhamnose.

Dr. K. Gadd, Director of the Public Health Laboratory, Department of Public Health, Lusaka, Northern Rhodesia, found that the tubers of *Dioscorea quartiniana* contain no hypoglycin A or B, but have a relatively high content of at least 14 amino acids, none of which is toxic (personal communication).

The Pharmacology and Toxicology of Species of *Dioscorea*

Boyd and Palmer¹² tested the expectorant effects of tinctures or liquid extracts of a number of plants, among them '*Dioscorea*', on some 500 animals, including cats, rabbits and guinea-pigs. '*Dioscorea*' (species not mentioned but apparently it was *D. villosa* L.) was administered in the form of a fluid-extract. The human dose of '*Dioscorea N.F.*' is 0.1 ml./kg. body weight. It produces only a moderate increase in the output of respiratory-tract fluid.

According to Bartlett,¹¹ '*Dioscorea*' is not a single species of *Dioscorea*, viz. *D. villosa* Linné. He states that 5 species, namely *D. floridana* Bartlett, *D. glauca* Muhl., *D. hirticaulis* Bartlett, *D. paniculata* Michx., and *D. quarternata* Gmel., have at times been identified as *D. villosa* Linné. These species of *Dioscorea* are all native to North America.

In large doses official '*Dioscorea*' (wild yam root, wild yam, colic root, rheumatism root, china root), induces nausea and may be expectorant and diuretic. It contains a saponin that is probably identical with '*dioscin*'.¹⁷

Discussing uterine sedatives and haemostatics, Sollmann²⁰ refers to *D. villosa* L. as giving 'more or less pronounced effects but not sufficient to confirm any therapeutic value'.

Broadbent and Schnieder²² compared some pharmacological properties of *dioscorine* and *dioscin* and the following is the discussion of their results:

'The pharmacology of *dioscorine* has been briefly described by Schutte (1897), Gorter (1911), and Leyva and Gutierrez (1937): A more detailed account has been given by Green (1953). He described picrotoxin-like convulsions and analeptic effects and estimated that the LD₅₀ for mice by intraperitoneal injection was 120 mg./kg., namely twice the value reported here. His observations that concentrations of 10⁻⁵ *dioscorine* did not affect the responses of isolated guinea-pig ileum to histamine and acetylcholine, and that doses of 20 mg./kg. of *dioscorine* did not alter the responses of the cat blood pressure to acetylcholine and adrenaline, differ from our findings.

'Precise comparisons between the two alkaloids are hampered by the instability of *dioscin* in aqueous solutions. However, our experiments show that *dioscorine* and *dioscin* have actions that are qualitatively similar, but that *dioscorine* is the more toxic and has greater local

anaesthetic activity, antidiuretic activity and depressant actions on the isolated guinea-pig ileum. Both resemble cocaine in causing potentiation of the pressor action of adrenaline on the cat blood pressure.

The most striking effect of the alkaloids, however, is the ability to cause convulsions, and this may be correlated with the convulsions that occur when alkaloid-bearing yams are eaten. The convulsions resemble those produced by picrotoxin and may be readily antagonized with pentobarbitone sodium (Broadbent and Reiff, 1956). Both alkaloids also resemble picrotoxin in possessing antidiuretic actions (Koiwa, 1939).

'We consider that our results are consistent with the view that the two alkaloids are closely related chemically.'

According to Codd,⁹ the cultivated yam belongs to the genus *Dioscorea*, comprising over 500 species distributed throughout the warmer countries of the world. He states that only 3 South African species of *Dioscorea* contain *diosgenin*, namely *D. elephantipes* Engl., *D. hemicypta* Burkill, and *D. sylvatica* L., and that no *diosgenin* is detectable in *D. retusa* Mast.

Abrol *et al.*¹⁰ made a pharmacognostic study of the rhizome of *Dioscorea deltoidea* Wall, which occurs abundantly in the north-western Himalayan region. The rhizome contains 2-8% of *diosgenin* and 'has now become a most important raw material for the synthesis of cortisone and steroid sex hormones'.

Van Itallie en Bylsma⁶ (p. 485) state that species of *Dioscorea* are one of the plants used as arrow poisons in the East Indies. They describe the symptoms of poisoning with *Dioscorea hirsuta* ('gadoeng') as follows: Burning sensation in the throat, gastric pain, vomiting, feeling of exhaustion, complete confusion. Death follows if a large amount of the tuber is eaten. The tuber can be rendered edible if it is extracted with water and then dried.

According to the *US Dispensatory*,¹¹ '*dioscin*' has a strong haemolytic action and a pronounced toxic effect on fish and amoebae.

'Dioscorine, C₁₃H₁₅O₂N, has been isolated from the tubers ('gadoeng') of *Dioscorea hirsuta* Blume and from the same organ ('nami') of *Dioscorea hispida* Dennst. which are indigenous to Batavia and the Tagalog provinces of the Philippines. Gadoeng and nami are used by the natives as a foodstuff after removal of the poisonous principle.¹² The method of extraction of *dioscorine* (a tropane alkaloid) is described.¹ When injected into monkeys, it has a mydriatic action, and in certain respects it resembles the pharmacological action of picrotoxin and cardiac glycosides (vagal stimulation).¹ Chemical reactions by which *dioscorine* can be identified are described by Holmes.²

DISCUSSION

Only women and children under 16 years of age (males and females) were affected

Here, as in other cases among Africans that I have investigated, the women and children go out to collect relishes and other wild foods while the men till the lands and build huts. On some occasions, children go out alone and collect relishes, or wander off into the fields or forests. They get hungry and are very much inclined to eat fruits, bulbs, tubers, or roots of plants. Poisonous plants are frequently confused with relishes or other edible plants, especially during droughts and winter months, when, as mentioned above, the above-ground portions of plants are dry and unidentifiable. This hazard becomes greatest to inhabitants who are unacquainted with the vegetation in the new areas in which they have settled. The digging up of tubers, roots, rhizomes, bulbs, etc., of which the above-ground portions are unidentifiable owing to paucity of the specimens, constitutes a special hazard. In South Africa the digging up of roots, etc. and the eating of wild fruits with which they were unacquainted, has been the cause of many cases of poisoning and death among both African and European adults and children. I am thinking particularly of the fruit and tubers of *Adenia digitata* Engl. (baboon poison), the fruits of *Acokanthera spectabilis* Hook. F. and *A. venenata* G. Don., the immature fruits

of certain *Cissus* spp., the tubers of *Neorautanenia ficifolia* (Benth.) C. A. Smith, the fruits (wild dates) of various species of *Encephalartos* (the outer fleshy portion is, as a rule, non-poisonous, while the kernels are a deadly liver poison), the immature (green) berries of *Solanum nigrum* L. (black nightshade), the leaves of certain *Cotyledon* spp. (these have recently caused the death of a few European children in the Carnarvon district), and the bulbs of poisonous species of *Moraea* and *Homeria* (tulips) which are confused with the bulbs of the edible *Moraea edulis*.

A point of interest is that it is the custom among African families to prepare their food in large iron pots. It is then divided between the women and the children under 16 years of age, who eat apart from the older men and the young males over the age of 16 years. This way of preparing and eating food is also being practised by the tribes resettled in the Lusito River area. This African habit points to the probability that the mysterious disease may have been, and probably was, caused by (1) the victims having eaten some toxic plant or plants in the raw state while out collecting relishes and other food plants in the forest, and (2) that the toxic principle(s) of such plants were destroyed by cooking. This would explain the fact that only the women and children who went out collecting relishes and food plants were affected and that the men and boys over 16 years of age, who ate only the cooked food, did not suffer. Cooking destroys the toxic principle of *Dioscorea quartiniana*.

Also, the fact that the women and children under the age of 16 years went out into the forest in the early morning when they were hungry and often only returned late in the day, would constitute a great inducement to them to still their hunger by eating the raw plants they were collecting. This would apply especially to the children. No wonder then that some children who had been quite well in the morning were found dead under trees or bushes later the same day.

The danger of confusing edible with toxic plants was indeed very great, because the affected area was drought-stricken at the time, with the result that it was extremely difficult, if not impossible, for the Africans to distinguish between edible and toxic plants which resembled each other. Also, owing to the great scarcity of food plants as a result of the severe drought, plants unknown to the stricken tribe may have been collected. This, I have often experienced in South Africa.

The Toxic Plants to be considered as Causes of the Mysterious Disease

These include the following:

Dioscorea quartiniana. There appears to be a great possibility that this plant was responsible for at least a fair percentage of the cases of poisoning, for two reasons:

1. In their abandoned homeland, the tubers of the non-toxic *Dioscorea schimperiana* constituted an important article of diet of the affected tribe, and
2. In their new homeland they found tubers (*Dioscorea quartiniana*) which resembled those they had eaten with impunity in their previous homeland. Unfortunately, owing to the paucity of the above-ground portions (runners, etc.) of the plant, as a result of the severe drought,

it was difficult for them to distinguish the one plant from the other.

Acalypha indica. This plant is very toxic owing to its high hydrocyanic-acid content (a cyanogenetic glucoside). It resembles several species of *Amaranthus* (pig-weed), which is known to the African as 'marôgo' and is, to them, a very popular relish (used as 'spinach'). Under certain conditions²² *Amaranthus* may contain such large amounts of nitrate that it also is fatal, especially to very young children. I have often seen Africans, young and old, and Bushmen, picking green weeds, including *Amaranthus*, and eating them in the raw state. Nitrate or nitrite poisoning is easily diagnosable, for its main symptom is methaemoglobinaemia.²² It is quite conceivable that at least some of the children who were found dead under the trees or bushes had consumed either *Acalypha indica* or *Amaranthus*, or both, and had died suddenly from peracute hydrocyanic-acid or nitrate poisoning. However, it is obvious that none of the cases in which an autopsy was performed (*unfortunately only a very small percentage of the fatal cases*), was a victim of either of these two plants, judging from the symptoms and postmortem appearances of the autopsied victims.

It is also possible that some of the victims, again especially children, had eaten cassava in the raw state with the result that they were poisoned by hydrocyanic acid.

I should add that all the adult Africans and children I saw, looked very well-fed. The responsible authorities had taken all the steps necessary for an adequate and wholesome supply of food and water and for the health of the resettled tribes.

CONCLUSION

From all the information supplied to me and collected by me during the course of my investigations into the cause(s) of the mysterious disease that had made its appearance in an African tribe in Northern Rhodesia in September 1959, it appears reasonable and feasible to conclude that the disease was caused by the eating, in a raw (*uncooked*) state, of one or more of the following plants: (A) *Dioscorea quartiniana*, (B) *Acalypha indica*, (C) species of *Amaranthus*, and (D) unknown poisonous plants.

In the past, I have frequently urged that cases of accidental poisoning like those described in this publication could be avoided, or at least reduced to a minimum, by educating and warning those, especially children, who are exposed to conditions apt to precipitate such tragic

events. Adequate education by exhibiting specimens or coloured pictures of the plants concerned (the poisonous as well as the edible) should be commenced in schools. This wise step was taken by Dr. Webster, Director of Medical Services, very soon after the first cases of this mysterious outbreak of disease had appeared.

This is especially important during dry periods and during winter and early summer months, when the plants are dormant and the above-ground portions very difficult, if not impossible, to identify.

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