

MUSHROOM POISONING

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The tragic cases of mushroom poisoning last year near Ermelo, Transvaal, again brought home to us the great danger of collecting and eating mushrooms with which we are not well acquainted.

Not only are there different species of poisonous mushrooms (fungi) but some edible kinds may, at times, induce allergic manifestations and, when decayed, may cause digestive disturbances and food poisoning. Further, in analogy with other poisonous plants, climatic and soil conditions may affect the toxicity of mushrooms.

Those who are concerned in the consumption of South African mushrooms are advised to consult the following publications: *Common Edible and Poisonous Mushrooms in South Africa*,⁵ by A. M. Bottomley and P. H. B. Talbot, and *Some South African Edible Fungi*,²²

and *Some South African Poisonous and Inedible Fungi*,²³ by Edith L. Stephens and M. M. Kidd.

If there is any doubt about the identity of a mushroom it may be submitted for identification to the head of the Division of Botany, P.O. Box 994, Pretoria, or to Miss Edith L. Stephens, c/o Bolus Herbarium, University of Cape Town, Cape Town.

VARIOUS TYPES OF MUSHROOM POISONING

Poisoning by mushrooms may be divided into 7 different types or groups:

1. *Old Decaying Mushrooms*

We fully agree with Miss Stephen's warning²² that only *fresh mushrooms* should be eaten because old

decaying ones may cause gastro-enteritis or food-poisoning.

Schöffling and Grosser¹⁹ report a case where freshly collected edible mushrooms were eaten with impunity, while the remaining quantity, which were eaten after having been kept in a warm kitchen for 24 hours, caused vomiting, cramps in the stomach and calves, and diarrhoea, within 12 hours. After 3 days treatment the patient recovered. The possible explanation is that at the high room-temperature either chemical decomposition or bacterial infection may have produced or liberated a poison or poisons.

2. Mushrooms causing allergic manifestations

As with many other foods, certain individuals may at times exhibit allergic manifestations (itching, urticaria, nausea, gastro-intestinal pains, and diarrhoea) after eating edible mushrooms. As a rule these reactions are of a transient nature and are quickly suppressed by the administration of alkaline laxatives (milk of magnesia), injections of adrenalin and synthetic antihistaminica, and intravenous injections of calcium gluconate.

3. 'Benign' Mushroom Poisoning

(a) Among the mushrooms causing 'benign' poisoning are many which contain poisons chemically related to resinic acid.¹⁹ As a rule they cause only transient gastro-intestinal disturbances (nausea, vomiting, and diarrhoea). However, if large quantities of them are eaten, life may be endangered, the chief complication being circulatory collapse. In Western Europe *Tricholoma pardinum* or *tigrinum* and *Entoloma lividum* are well-known representatives of this group of mushrooms.¹⁹ In South Africa *Clitocybe olearia* (copper trumpet),²³ *Hebeloma crustuliniforme* (poison pie),²³ *Lepiota morgani* (green-lined parasol)^{5,23} and *Psalliota xanthoderma* (yellow-staining mushroom)^{5,9,23} may cause severe gastro-intestinal irritation (nausea, vomiting, diarrhoea, and headaches). The active principles are unknown. Symptoms set in within 1-6 hours after eating. Treatment is symptomatic after the gastro-intestinal tract had been emptied by stomach lavage and purgatives.

(b) Schöffling and Grosser¹⁹ refer to another type of 'benign' mushroom-poisoning which sets in only when certain mushrooms are eaten and alcohol is consumed at the same time or immediately afterwards. In Germany the so-called *Faltentintling* is an example of this type of mushroom poisoning. The symptoms closely resemble those of nitrite poisoning, viz. dizziness, headache, reddening of skin of the head and chest, lowered blood pressure, tachycardia, and increased respiration. Treatment is symptomatic. According to Dr. B. J. Chohnoky of the Department of Botany, University of Pretoria, various species of *Hebeloma* and *Armillaria* are called *Faltentintling* in Germany.

4. Mushrooms containing (a) muscarine and (b) muscarine and myceto-atropine

(a) *Muscarine*. Poisoning by mushrooms containing muscarine is well known.^{5,9,19,20,21,23,27} The symptoms are essentially those of stimulation of the parasympa-

thetic nervous system, viz. hyperhidrosis, profuse salivation, spasms of coughing, respiratory distress, miosis, visual disturbances (accommodation), bradycardia followed by tachycardia, pronounced gastro-enteritis, suppression of consciousness, and muscle tremors. Treatment includes the use of the stomach pump, adsorbents and laxatives, plus symptomatic treatment. *Of the greatest value is the use of atropine, the pharmacological antidote to muscarine.* Atropine sulphate should be used in 1.0 mg. doses, repeated if necessary. In very serious cases atropine sulphate should be administered by *slow* intravenous injection. The 3 representatives of this group of mushrooms are *Inocybe eutheles*, *I. hirtella* and *I. obscura*.²³ Poisoning by these muscarine-containing mushrooms is not so dangerous and deadly as that induced by *Amanita phalloides* and *A. Capensis* (which are both severe liver poisons) because vomiting is an early symptom, appearing within ½-4 hours after consumption, thus ridding the victim of a large proportion of the poison.

(b) *Muscarine and myceto-atropine*.^{5,19,23} *Amanita muscaria* (the fly agaric) and *A. pantherina* (the panther) represent this group. Botanically the two are closely related; in early times they were used to kill flies. They present the interesting phenomenon that they contain two pharmacological or toxicological antagonists, namely, muscarine which is parasympathomimetic and myceto-atropine which is parasympatholytic. (Lewis^{16(a)} isolated a substance with the properties of l-hyoscyamine from Cape *A. muscaria* and *A. pantherina*). Consequently, poisoning by these two mushrooms does not always present the same picture, for the symptoms depend on the relative quantities of the two poisons present. If muscarine is present in larger quantities than mycetoatropine, symptoms of stimulation of the parasympathetic nervous system will supervene, as described under muscarine; while if myceto-atropine is in excess, symptoms of atropine poisoning will be in evidence. In the latter case the following symptoms appear from about 1-4 hours after eating the mushrooms: Dryness of the mouth and throat accompanied by a hoarse voice, mydriasis, burning pain in the stomach, dizziness, vomiting, diarrhoea, and stimulation of the central nervous system (excitation, hallucinations, delirium, mania, muscle tremors, and spasm) followed by coma. The symptoms of stimulation of the gastro-intestinal tract are caused by the muscarine which is present. As a rule the symptoms disappear within 12-16 hours. In this type of mushroom poisoning the prognosis is usually good in spite of the serious symptoms. Treatment consists in emptying the gastro-intestinal tract, unless severe vomiting and diarrhoea have already occurred, and in symptomatic treatment. It is not advisable to administer atropine antagonists (neostigmine, carbachol etc.), because they may aggravate the muscarine symptoms. However, if the symptoms of atropine are so pronounced that life is endangered, small quantities of parasympathomimetics should be administered at short intervals until the symptoms are controlled.

If muscarine and myceto-atropine are present in such quantities that these two antagonists neutralize each

other, symptoms of poisoning will be slight or absent.

According to Steidle²¹ the statement that has been made that only the skin of *A. muscaria* and *A. pantherina* is poisonous, is false and dangerous. The quantities of muscarine he found in *A. muscaria* was as follows: Skin 0.034%, cap+gills 0.026%, bulb 0.029%, and in the stem only traces. In *A. pantherina* also he found muscarine more concentrated in the skin than in other parts.

Kwasniewski¹⁵ agrees with Tschirch that muscarine does not occur in fresh specimens of *A. muscaria*, but is formed during cooking or during the processes of isolation from the mushrooms. Nencki (Kwasniewski¹⁵) was also unable to detect muscarine in fresh *A. muscaria* and maintains that this poison is liberated during cooking.

5. Mushrooms containing helvellic acid

Aye,¹ Kämpf,¹² Kärber,¹³ Landé,^{15a} Reif,^{17a} Schöffling and Grosser,²⁰ and Stulfauth and Jung²⁵ refer to poisoning with *Helvella esculenta*. The only poison known to occur in this mushroom is helvellic acid, which has been isolated by Boehm and Külz (Schöffling and Grosser²⁰)—not to be confused with helvolic acid, an antibiotic isolated by Chain *et al.*⁶ from the fungus *Aspergillus fumigatus*.

Helvellic acid causes haemolysis in animals, which, however, is practically never seen in human beings after eating this mushroom. The acid is volatile and destroyed by boiling, and apparently drying and boiling renders this mushroom edible. The water in which the mushroom is cooked should be discarded and not used for the preparation of gravy or soup. The addition of salt or steeping the mushroom in vinegar is said not to destroy the helvellic acid contained in it.

Kämpf¹² was able to diagnose a case of *H. esculenta* poisoning by preparing an extract of the contents of the colon of the victim, and by means of 3 colour tests identifying in the extract certain volatile, reducing, aldehyde-like substances that are present in this mushroom.

From the literature it appears possible that, at times, *H. esculenta* may also contain a toxic principle identical with, or chemically related to amanitine or phalloidine (contained in *A. phalloides* and *A. capensis*), because the long period of latency (6-24 hours) as well as the symptoms of poisoning in some of the victims has resembled those seen in poisoning with *Amanita*. Icterus may appear only on the 2nd or 3rd day after the appearance of symptoms. At autopsy haemsiderosis has been seen at both *H. esculenta* and *A. phalloides* poisoning. Stulfauth and Jung²⁵ state that *H. esculenta* is primarily a liver poison.

H. esculenta is not known to occur in South Africa, but *H. mitra* has been recorded by Dr. E. M. Doidge⁷ as occurring in the Cape. To our knowledge nothing is known about the possible danger of this species of *Helvella*, but the fact that the poisonous *H. esculenta* is sometimes eaten with impunity, must serve as a warning that *H. mitra* may at times be poisonous.

6. Mushrooms containing amanitine and phalloidine

In South Africa two mushrooms representing this

group are known, viz. *A. capensis* Pearson and Stephens ('Kaapse amaniet', Cape death-cup) and *A. phalloides* ('duiwelsbrood', 'doodsbekerswam', death cup).^{5,23} Of all poisonous mushrooms they are by far the most deadly, for the reason that (1) the active principle amanitine (amanitotoxin) is a severe liver-poison and (2) the symptoms of poisoning appear only 6-48 hours after ingestion of the mushrooms, when serious damage has already been done to the liver and other organs. Poisoning by *A. phalloides* is extensively referred to in the literature.^{3,4,5,8-11,14,16,17,18,20,23,26,28}

Active principles of A. phalloides. Wieland *et al.*²⁸ review the history of the attempts to isolate the active principles of this mushroom. These investigators found that the LD/100 of α -amanitine for mice amounted to 0.2 μ g per g. body-weight. Death resulted in an average of 5 days. This fatal period was reduced to 15 hours by administering 200 times the fatal dose. The poison was administered intravenously and subcutaneously. Hoechstetter and others (Dubash and Teare⁸) state that this mushroom contains 2 toxins, viz. (1) a thermostable toxin (amanitine) with a phosphorus-like action, and (2) a thermolabile one (phallin or phalloidine¹⁴) a haemolysin, which is rapidly destroyed by digestive juices, weak acids, alkalis, and heat. Ford and Prouty¹¹ state that drying does not destroy amanitine, which is the toxin responsible for the severe liver damage. Phalloidine (phallin)¹⁴ does not cause poisoning since it is destroyed by heat, but when it is administered parenterally it causes haemolysis. Possibly, if the mushrooms are not well cooked some haemolysin may be retained and may induce haemolysis. According to Dubash and Teare⁸ numerous attempts have been made to produce an antiserum against *A. phalloides*. As early as 1897 Calmette succeeded in increasing the resistance of rabbits to this mushroom by previously injecting them with an extract prepared from the macerated fungus. In 1933 de le Rivière produced antiphalloidine serum by injecting a horse with extracts of the fungus and apparently achieved good results by administering this serum within a reasonable time after the onset of symptoms.

Symptoms of poisoning of A. phalloides and A. capensis. Within 6-24 hours or more after ingestion the following symptoms suddenly appear: Acute pains in the abdomen, persistent vomiting and pronounced (frequently haemorrhagic or cholera-like) diarrhoea accompanied by tenesmus. If suitable treatment is not immediately instituted, the pronounced loss in water and electrolytes induces exsiccation, cramps in the calves, and extra-renal azotaemia and uraemia. In such cases the victims may die on the 3rd day from cardiovascular collapse in a state of coma and with symptoms of cerebral stimulation; but with suitable treatment the symptoms of gastro-intestinal irritation may subside, or even completely disappear, within a few days. However, in the majority of cases symptoms of severe liver-damage appear within 3-5 days after ingestion and the following symptoms are then exhibited: Nausea, vomiting, general icterus (acute yellow atrophy of the liver), haemorrhagic diathesis, and coma hepaticum. Miosis

or mydriasis may be present, more often the latter. Carbohydrate metabolism is disturbed and an initial increase in blood sugar is followed by hypoglycaemia. The damaged liver is unable to synthesize glycogen from glucose. Haemolysis is extremely rare. Approximately 50% of these cases end fatally within 7 to 8 days. Mortality is very high, ranging from 35 to 80%.

Immediate emptying of the stomach (stomach pump) and intestines (purgatives) is of life-saving value. It should be kept in mind that alcohol favours absorption of *amanitine*, and consequently aggravates poisoning.

Meusel *et al.*¹⁷ report favourable results in cases of *A. phalloides* poisoning by continuous intravenous infusion of 1 litre of a 0.001 to 0.002% solution of choline.

Pathology and histology. At autopsy the picture closely resembles that seen in poisoning with yellow phosphorus. There is opaque swelling of the enlarged liver with diffuse fatty degeneration and partial necrosis of the parenchyma cells, the kidneys show fatty degeneration of the tubule epithelium, and there is fatty degeneration of the cardiac muscle with numerous haemorrhages on the serous and mucous membranes.

7. Mushrooms containing *amanitine*, *phalloidine* and *muscarine*

It appears that at times certain mushrooms, e.g. *Lepista cafferorum* (Kalchbr. and MacOwan Singer),²⁴ may contain a mixture of poisons affecting the liver and stimulating the parasympathetic nervous system. The former poisons may be identical with, or chemically closely related to, *amanitine* and *phalloidine* (*A. phalloides*) and the parasympathomimetic substance(s) may be identical with, or chemically related to, *muscarine*.

THE ERMELO CASES

During February 1955 one of us (D.W.S.) attended 9 cases—8 European (4 adults and 4 children) and 1 Bantu—of *Amanita phalloides* poisoning near Ermelo, district Transvaal. The 4 European adults recovered after having exhibited very serious symptoms of poisoning, and the remaining 5 cases ended fatally.

(a) The European Cases

The 8 European patients were comprised in 2 families, viz. a young married couple (Mr. and Mrs. A.), and a married couple (Mr. and Mrs. B.) with 4 children (a girl aged 7 years, a boy aged 6 years, and twins aged 3½ years; a fifth child—a girl of 15 years—was visiting friends at the time and was not involved in the tragedy).

On Sunday 13 February 1955 a prolific growth of mushrooms was seen under the oak trees of the Government Experimental Farm, Nooitgedacht (3 miles east of Ermelo) adjoining the homesteads of the families A and B, who were neighbours. During the preceding 3 weeks continuous and heavy rains had fallen and the last 2 days were hot and sunny. The B family were invited by the A family to come and gather mushrooms with them, and at first declined on the ground that they were not able to recognize poisonous mushrooms. They were, however, reassured by the A family, who said they came from the Cape and were well acquainted

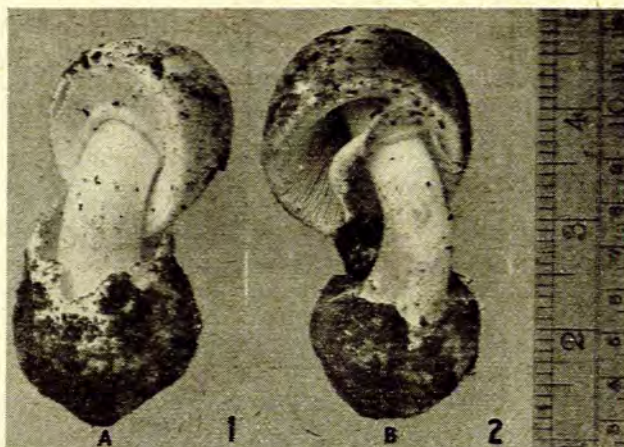


Fig. 1. *Amanita phalloides* (Vaill. ex Fr.) Secr.: Showing two immature plants with ruptured vortex (hence the name 'death cup') and the veil (1) commencing to rupture, and (2) partially torn from the gills. *Locality*: Under oak trees on the farm Nooitgedacht, 3 miles east of Ermelo, Transvaal, where the cases of mushroom poisoning referred to in this article, had occurred.

with the poisonous kinds of mushroom; and between 10 and 11 a.m. on 13 February the two families picked a basketful of the mushrooms growing under the oak trees. These were fried in butter and eaten at 12 noon the same day by 8 individuals of the two families. Unfortunately, it is impossible to state the approximate quantities of mushrooms eaten by the patients.

Symptoms of poisoning (extreme nausea, persistent vomiting and watery diarrhoea, and severe abdominal cramps) set in at 12 midnight, i.e. approximately 11 to 12 hours after consumption of the mushrooms, in all the 8 persons who had partaken of them.

Monday 14 February. All patients exhausted and weak in addition to the above symptoms. Mrs. A. complained that her eyesight was bad. Accelerated pulse, dehydration and shock. All the 8 patients showed pronounced miosis and all of them complained of increased salivation (possibly due to the presence of a small percentage of *Amanita muscaria* in the basket of *A. phalloides*). Epigastric area was sensitive to pressure and a pronounced increase in intestinal peristalsis could be detected. No signs of general icterus, sensitivity of the liver to pressure, or increase in the size of this organ at this stage. All cases were hospitalized and given intravenous infusions of 5% glucose in saline with 200 mg. of vitamin C+200 mg. of vitamin B₆+2.0 c.c. of Bejectal (vitamin B complex)+vitamin K. Furthermore each patient received an intravenous injection of atropine sulphate (adults 1/70th gr. and the children 1/150th gr.). Within 10 minutes of the injection there was an improvement in the vomiting and diarrhoea and the contracted pupils increased in size. It was found necessary to repeat the atropine injections in some cases as stimulation of the parasympathetic nervous system, due to muscarine, was again in evidence when the effect of atropine had worn off. Toward the Monday evening all the patients showed a fair degree of improvement. Restlessness in the children was treated with intramuscular injections of paraldehyde.

Tuesday 15 February. All the patients had had a good night and their condition had improved. In the evening the 4 children showed enlarged livers which were sensitive to pressure; restlessness was so pronounced that repeated injections of paraldehyde had to be given.

Wednesday 16 February. The 4 children showed subnormal temperatures (95°-96°F), stupor, and yellowish sclerae. All showed pronounced enlargement of the liver, which was very sensitive to pressure. The urine was dark in colour (positive

reaction for bile and, in one case, also positive for protein). All 4 children died in the course of the afternoon and evening. They showed terminal stupor, coma and convulsions. Approximately 6 hours before death they all vomited dark-coloured blood. The adults also exhibited slight scleral icterus and their livers were sensitive to pressure.

Thursday 17 February. The 4 adults showed more pronounced scleral icterus and in all cases the liver was markedly enlarged and very sensitive to pressure. Mr. A also exhibited a yellowish skin and bile was present in his urine. Two of the patients showed albuminuria. Vomiting and diarrhoea had improved. Since the previous evening the 4 adults received the following treatment: Litrison tablets (Roche product containing methionine, choline, B-complex vitamins and vitamin E), 2 tablets 3 times daily; 2 Multivitamine tablets 3 times daily; intramuscular injections of Bejectal (B complex), 2 c.c. and vitamin K, 5.0 mg., twice daily; pethidine, 100.0 mg. intramuscularly, as required for abdominal pain; intravenous calcium gluconate+dextrose; Kaopectin, fruit juice, and light fat-free meals.

Friday 18 February. Scleral icterus more pronounced in all 4 patients. Increase in enlargement of liver, which was also much more sensitive to pressure. Skin of Mr. A yellowish in colour while his urine was dark in colour and showing a positive reaction for bile and protein. Temperatures showed a tendency to become subnormal and the pulses varied markedly in strength and rate.

Saturday 19 February. Mr. A showed a temperature of 95°F and an increasing degree of stupor. In the afternoon he was unconscious. Pronounced general icterus. Previous treatment continued. The condition of the remaining 3 patients improved; also the icterus.

Sunday 20 February. Mr. A still in coma; catheterization was necessary. Increase in dextrose and calcium gluconate intravenously administered. Temperature 95°F. Toward evening his temperature rose to 97° and the corneal reflex reappeared for the first time. The improvement in the condition of the remaining 3 patients continued; their appetite also improved. The above treatment was continued.

Monday 21 February. Mr. A began to regain consciousness and ate a little, but there was still a pronounced degree of icterus. Sensitivity of liver to pressure less marked. Urine still dark and positive for bile; trace of albumen present. Progressive improvement in the condition of the remaining 3 patients. The intravenous injections were discontinued.

In the course of the following week all the patients showed such improvement that the last one was discharged from hospital on Sunday 27 February.

Mrs. B did not return to normal health but continued to vomit and showed progressive weakness. Subsequent examination, however, revealed that she was suffering from an internal trouble not associated with the mushroom poisoning.

(b) The non-European Patient

At midday on Thursday 10 February 1955 the Bantu patient collected and ate an unknown quantity of raw *Amanita phalloides* on another farm, Arcadia, adjoining Ermelo town. At midnight, approximately 12 hours after ingestion of the mushrooms, the patient developed symptoms very similar to those described in the above European patients. He was admitted to the same hospital as the other patients on 11 February and was treated on similar lines. He died in a coma on 16 February.

Post-mortem Appearances

Liver. Enlarged and yellow and of firm consistence. Fatty degeneration.

Myocardium. Flabby, soft and yellowish in colour.

Kidneys. Flabby and soft, petechiae in cortex.

Gastro-intestinal Tract. Areas of erosion, with haemorrhages, in the gastric mucosa. Contents of entire gastro-intestinal tract brownish in colour (changed blood).



Fig. 2. *Amanita phalloides* (Vaill. ex Fr.) Secr.: Mature plant clearly showing the remains of the ruptured veil and vortex ('death cup'). *Locality:* Under oak trees on the farm Arcadia, in the immediate vicinity of Ermelo, Transvaal, where a Bantu man died from eating this mushroom.

The remaining organs showed no macroscopic changes.

Unfortunately no specimens were submitted for histological examination.

Comment

This was the first occasion on which poisoning with *Amanita muscaria* or *A. phalloides* had been recorded in the Transvaal. The explanation of this rarity probably lies in the fact that the Transvaal is a summer-rainfall area characterized by sudden violent rainstorms following which the ground surface dries off quickly. Climatic conditions are therefore usually unfavourable to heavy growth of mushrooms; but during the 3 weeks before the occurrence of these cases of poisoning continuous and heavy rains fell in the Ermelo district, and humidity and atmospheric temperatures were fairly high. These conditions were very favourable to the growth of mushrooms, and masses of *A. phalloides* and other mushrooms, including a few *A. muscaria*, were found growing under oak trees, as they often do in other countries.

Biological Tests

Biological tests were conducted upon rabbits with material of *Amanita phalloides* collected on the spot from which the two European families obtained the mushrooms they had eaten. The fresh material proved to be extremely poisonous and caused symptoms and pathological changes in the liver and kidneys of the

rabbits* very similar to those described in human beings. The minimum lethal dose was approximately 1.0 g. per kg. body-weight. An interesting phenomenon was that the smallest lethal quantity of mushroom killed the rabbits 16 hours after administration and the largest quantity (60.0g. per kg. given in the course of 4 hours) caused death in 9 hours; no matter how large the dose, the interval between administration and death could not be reduced to below 9 hours. Krause's conclusion¹⁴ that rabbits can eat *A. phalloides* without harm is incorrect. The same applies to his remark¹⁴ that guinea pigs are insusceptible to amanitine, for Renz¹⁸ used these animals in his attempts to purify amanitine and Verne²⁶ found extracts of *A. phalloides* toxic to rats and guinea pigs.

SUMMARY AND CONCLUSION

Seven different types of poisoning by mushrooms are described, and also the cases of mushroom poisoning form *Amanita phalloides*, which occurred near Ermelo, Transvaal, in February 1955 when a Native and 4 children in one European family died. This tragic event must serve as a serious warning to everybody not to eat any mushrooms with which they are not thoroughly acquainted.

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