

Curare

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Curare /kjuːˈrɑːriː/^[1] is a common name for various arrow poisons originating from South America. The three main types of curare are:

- tubocurare (also known as tube or bamboo curare, because of its packing into hollow bamboo tubes; main toxin is D-tubocurarine). It is a mono-quaternary alkaloid, an isoquinoline derivative.
- calebas curare (also called "gourd curare" by older British classifications, being packed into hollow gourds; main toxins are alloferine and toxiferine)
- pot curare (packed in terra cotta pots; main toxins are protocurarine, protocurine, and protocuridine).

Of these three types, some formulas belonging to the calebas curare are the most toxic, relative to their LD₅₀ values.



Strychnos toxifera by Koehler
1887

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History

Curare was used as a paralyzing poison by South American indigenous people. The prey was shot by arrows or blowgun darts dipped in curare, leading to asphyxiation owing to the inability of the

victim's respiratory muscles to contract. The word curare is derived from *wurari*, from the Carib language of the Macusi Indians of Guyana.^[2]

In 1596 Sir Walter Raleigh mentioned the arrow poison in his book *Discovery of the Large, Rich, and Beautiful Empire of Guiana* (now Guyana), though it is possible that the poison he described was not curare.^[3] In 1780, Abbe Felix Fontana discovered that it acted on the voluntary muscles rather than the nerves and the heart.^[4] In 1800, Alexander von Humboldt gave the first western account of how the toxin was prepared from plants by Orinoco River natives.^[5]

During 1811-1812 Sir Benjamin Collins Brody (1783–1862) experimented with curare.^[6] He was the first to show that curare does not kill the animal and the recovery is complete if the animal's respiration is maintained artificially. In 1825 Charles Waterton described a classical experiment in which he kept a curarized female donkey alive by artificial respiration with a bellows through a tracheostomy.^[7] Waterton is also credited with bringing curare to Europe.^[8] Robert Hermann Schomburgk, who was a trained botanist, identified the vine as one of the *Strychnos* genus and gave it the now accepted name *Strychnos toxifera*.^[9]

George Harley (1829–1896) showed in 1850 that curare (wourali) was effective for the treatment of tetanus and strychnine poisoning.^{[10][11]} From 1887 the Burroughs Wellcome catalogue listed under its 'Tabloids' brand name, tablets of curare at 1/12 grain (price 8 shillings) for use in preparing a solution for hypodermic injection. In 1914 Henry Hallett Dale (1875–1968) described the physiological actions of acetylcholine.^[12] After twenty-five years he showed that acetylcholine is responsible for neuromuscular transmission, which can be blocked by curare.^[13]

The best known and historically most important (because of its medical applications) toxin is d-tubocurarine. It was isolated from the crude drug — from a museum sample of curare — in 1935 by Harold King (1887–1956) of London, working in Sir Henry Dale's laboratory. He also established its chemical structure.^[14] It was introduced into anesthesia in the early 1940s as a muscle relaxant for surgery. Curare is active — toxic or muscle-relaxing, depending on the intended use — only by an injection or a direct wound contamination by poisoned dart or arrow. It is harmless if taken orally^{[7][15]} because curare compounds are too large and highly charged to pass through the lining of the digestive tract to be absorbed into the blood. For this reason, native tribes are able to eat curare-poisoned prey safely. In medicine, curare has been superseded by a number of curare-like agents, such as rocuronium, which have a similar pharmacodynamic profile but fewer side effects.

The U2 spy-plane pilot Gary Powers, when shot down in 1960 on his flight over the Soviet Union, was wearing a silver-dollar charm that concealed a curare-tipped needle.

Pharmacological properties

Curare is an example of a non-depolarizing muscle relaxant that blocks the nicotinic acetylcholine receptor (nAChR), one of the two types of acetylcholine (ACh) receptors. The main toxin of curare, d-tubocurarine, occupies the same position on the receptor as ACh with an equal or greater affinity, and elicits no response, making it a competitive antagonist. The antidote for curare poisoning is an acetylcholinesterase (AChE) inhibitor (anti-cholinesterase), such as physostigmine or neostigmine. By blocking ACh degradation, AChE inhibitors raise the amount of ACh in the neuromuscular junction; the accumulated ACh will then correct for the effect of the curare by activating the receptors not blocked by toxin at a higher rate.

Anesthesia

Isolated attempts to use curare during anesthesia date back to 1912 by Arthur Lawen of Leipzig,^[16] but curare came to anesthesia via psychiatry (electroplexy). In 1939 Abram Elting Bennett used it to modify metrazol induced convulsive therapy.^[17] Muscle relaxants are used in modern anesthesia for many reasons, such as providing optimal operating conditions and facilitating intubation of the trachea. Before muscle relaxants, anesthesiologists needed to use larger doses of the anesthetic agent, such as ether, chloroform or cyclopropane to achieve these aims. Such deep anesthesia risked killing patients that were elderly or had heart conditions. The source of curare in the Amazon was first researched by Richard Evans Schultes in 1941. Since the 1930s, it was being used in hospitals as a muscle relaxant. He discovered that different types of curare called for as many as 15 ingredients, and in time helped to identify more than 70 species that produced the drug.

On January 23, 1942, Dr. Harold Griffith and Dr. Enid Johnson gave a synthetic preparation of curare (Intercostrin/ Intocostrin) to a patient undergoing an appendectomy (to supplement conventional anesthesia). Curare (d-tubocurarine) is no longer used for anesthesia during surgery as better drugs are now available. When used with halothane d-tubocurarine can cause a profound fall in blood pressure in some patients as both the drugs are ganglion blockers.^[18] However, it is safer to use d-tubocurarine with ether.

In 1954, a sensational article was published by Beecher and Todd suggesting that the use of muscle relaxants (drugs similar to curare) increased death due to anesthesia nearly sixfold.^[19] This has been completely disproven.

Modern anesthetists have at their disposal a variety of muscle relaxants for use in anesthesia. The ability to produce muscle relaxation independently from sedation has permitted anesthetists to adjust the two effects separately as needed to ensure that their patients are safely unconscious and sufficiently relaxed to permit surgery. The use of neuromuscular blocking drugs carries with it a

very small risk of anesthesia awareness.

Plants from which primary components of curare can be extracted

- *Strychnos toxifera*
- *Chondrodendron tomentosum*

Names

Curare is also known as Ampi, Woorari, Woorara, Woorali, Wourali, Wouralia, Ourare, Ourari, Urare, Urari, and Uirary.

d-Tubocurarine, the popular alkaloid of Curare used as a medicine.

Notes

1. ^ "curare". *Oxford English Dictionary*. Oxford University Press. 2nd ed. 1989.
2. ^ <http://www.etymonline.com/index.php?term=curare>
3. ^ Carman J. A. *Anaesthesia* 1968, **23**, 706.
4. ^ The Gale Encyclopedia of Science. Third Edition.
5. ^ [1] (<http://www.gutenberg.org/etext/7014>) *Personal Narrative of Travels to the Equinoctial Regions of America, During the Year 1799-1804 — Volume 2*, Humboldt, Alexander von
6. ^ *Phil. Trans.* 1811, **101**, 194; 1812, **102**, 205.
7. ^ **a b** Arrow Poison to Surgical Muscle Relaxant (<http://www.yeoldehog.com/medicinal/curare.shtml%7CFrom>)
8. ^ Reprinted in "Classical File", *Survey of Anesthesiology* 1978, **22**, 98.
9. ^ Waterton and Wouralia. *British Journal of Pharmacology* (1999) 126, 1685–1689 (<http://www.nature.com/bjp/journal/v126/n8/full/0702409a.html>)
10. ^ Paton A. *Practitioner* 1979, **223**, 849
11. ^ George Harley (<http://www.whonamedit.com/doctor.cfm/3230.html>)
12. ^ Dale H. H. *J. Pharmac. Exp. Ther.* 1914, **6**, 147.
13. ^ Dale H. H. *Br. Med. J.* 1934, **1**, 835
14. ^ King H. J. *Chem. Soc.* 1935, **57**, 1381; *Nature, Lond.* 1935, **135**, 469.
15. ^ Curare - *Chondrodendron tomentosum* (<http://www.blueplanetbiomes.org/curare.htm>)
16. ^ Lawen A. *Beitr. klin. Chir.* 1912, **80**, 168.
17. ^ Bennett A. E. *J. Am. Med. Ass.* 1940, **114**, 322
18. ^ Mashraqui S. Hypotension induced with d-tubocurarine and halothane for surgery of patent ductus arteriosus. *Indian Journal of Anesthesia*. 1994 Oct; 42(5): 346-50
19. ^ Beecher H. K. and Todd D. P. (1954). "A Study of the Deaths Associated with Anesthesia and Surgery : Based on a Study of 599,548 Anesthesias in Ten Institutions 1948-1952, Inclusive" (<http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pmcentrez&artid=1609600>) . *Ann. Surg*

(reprinted in "Classical File", *Survey of Anesthesiology* 1971, **15**, 394, 496) **140** (2): 2–35.
PMC 1609600 (<http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=1609600>) .
PMID 13159140 (<http://www.ncbi.nlm.nih.gov/pubmed/13159140>) .
<http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pmcentrez&artid=1609600>.

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External links

- Charles Waterton's book **Wanderings in South America** Free version (<http://infomotions.com/etexts/gutenberg/dirs/etext05/7wnsa10.htm>)
- Neuromuscular blocking drugs: discovery and development (<http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1279945>})

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