

The proposal to designate Cholera toxin as this month's poison...

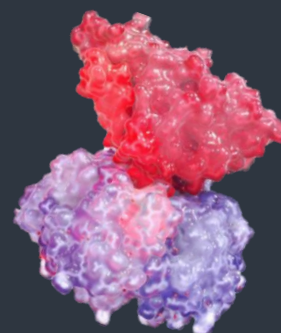
came from Professor Holger Barth, director of the Institute for Experimental and Clinical Pharmacology, Toxicology, and Naturopathy at Ulm University Hospital and chairman of the GT Working Group on Biogenic Toxins. The focus of his research is the investigation of the interaction of various proteins in functional complexes that collectively mediate the transport of proteins across cell membranes. In this regard, bacterial toxins serve as ideal models for highly specialized and extremely efficient protein transport machines acting within human cells.

Biogenic toxins

Are chemical compounds produced by microorganisms such as bacteria and algae, as well as by fungi, plants, or animals, which are harmful or even lethal to other organisms. Biogenic toxins are mainly produced through secondary metabolism and are therefore not essential for the organism's survival. They primarily serve defense purposes, such as protection against predation. Some animals also use their toxins to paralyze or kill prey. The effectiveness of biogenic toxins on various organisms varies greatly, as it depends on factors such as the method of uptake, the metabolism of the organism in question, and its sensitivity.

Enterotoxins

Enterotoxins are toxic substances produced by microorganisms that exert their harmful effects in the gastrointestinal tract. They are cytotoxic proteins that typically alter the permeability of epithelial cells in the intestinal mucosa by forming pores in the cell membrane, leading to cell death. As a result, gastroenteritis may occur.



Cholera toxin

Cholera - despite knowledge of the danger, still on the rise.

In late February, about 3000 people were stranded on a cruise ship in the Caribbean. Neither La Réunion nor Mauritius authorities granted entry to the travellers. The reason for this drastic action was an increased incidence of gastrointestinal illnesses on board the ship, prompting investigation into whether the illnesses were caused by the cholera pathogen. Fortunately, this suspicion did not hold true for the ship coming in from Africa, providing relief for the travellers.

Unfortunately, this does not apply to large parts of southern Africa and the Indian subcontinent. Rising numbers of cholera infections, as well as countries reporting new cholera outbreaks, contribute to a globally tense situation. In 2023, the World Health Organization (WHO) estimated 667,000 cases of illness and approximately 4,000 deaths.

Cholera is an acute bacterial gastrointestinal infection caused by the bacterium *Vibrio cholerae*. *Vibrio cholerae* is a gram-negative, rod-shaped bacterium from the family Vibrionaceae.

Upon entering the intestine, *Vibrio cholerae* produces an enterotoxin called Cholera toxin. The toxin is mainly produced during the bacterium's exponential growth phase when it actively multiplies and is present in sufficient numbers.

Cholera toxin is a protein molecule complex consisting of one A subunit and five identical B subunits. These subunits work together to exert the toxin's effects on the body.

The B subunit of Cholera toxin is responsible for binding to specific cell surface receptors, particularly those on the surface of intestinal epithelial cells in the small intestine.

This binding enables the internalization of the toxin into the cells (endocytosis). Once the Cholera toxin has been taken up by the cell, the A subunit is released, which is responsible for the toxicity.

Bacterial protein toxins

Cholera toxin belongs to the group of bacterial protein toxins. Bacterial protein toxins are the most toxic substances known and direct triggers of numerous life-threatening diseases in humans. Therefore, they represent important drug targets, and the search for inhibitors to suppress their toxic effects is of high scientific and medical relevance.

Cholera Infection

The natural reservoir for *Vibrio cholerae* is surface water, including seawater. Most outbreaks are reported from tropical and subtropical countries. Infection with *Vibrio cholerae* usually occurs through contaminated drinking water, feces, vomit from sick individuals, or consumption of contaminated food. Natural disasters such as floods or tsunamis can also lead to cholera outbreaks due to the breakdown of water supply and the mixing of sewage and drinking water.

The time between infection and the onset of illness is a few hours and usually no longer than 2-3 days.

Prevention and Vaccination

"Cook it, boil it, peel it, or forget it!" is an important guideline for handling food in areas where cholera infections cannot be ruled out.

In Germany, the oral inactivated vaccine Dukoral is approved, which is generally well-tolerated. In other countries, attenuated live vaccines against cholera are also approved.

The A subunit contains an enzymatic domain that possesses ADP-ribosyl transferase activity, initiating a signalling cascade within the cell. It catalyses the transfer of ADP-ribose to a G protein, leading to the permanent activation of the G protein. The sustained activation of the G protein excessively stimulates adenylate cyclase, resulting in the overproduction of cyclic adenosine monophosphate (cAMP) in the cells of the small intestine. As an important second messenger, cAMP influences ion transport across the cell membrane. Specifically, it activates chloride channels and inhibits the sodium-potassium pump. The result is a massive excretion of chloride ions along with the inhibition of sodium ion reabsorption. This leads to significant salt (NaCl) and fluid loss in the intestine, resulting in the characteristic watery diarrhoea associated with cholera infection.

Affected individuals can lose up to 2 liters of fluid per hour, experiencing a life-threatening electrolyte imbalance, which can lead to kidney failure, circulatory collapse, and death.

However, the majority of cholera infections are asymptomatic or mild. Nevertheless, these individuals can still shed bacteria for up to ten days after infection, which can enter the water cycle and infect other people, further facilitating the spread of cholera.

Text: Ute Haßmann

Literature and links:

- [Forschungsfelder | Universitätsklinikum Ulm \(uniklinik-ulm.de\)](#)
- [Keine Cholera auf Kreuzfahrtschiff vor Mauritius | tagesschau.de](#)
- [Cholera \(who.int\)](#)
- [Weltweit rund 667.000 gemeldete Cholerafälle \(aerzteblatt.de\)](#)
- [Tropeninstitut - Impfung - Cholera](#)
- Foto of [Tony Lam Hoang](#) on [Unsplash](#)
- [www.MedicalGraphics.de: Lizenz CC BY-ND 4.0 DE](#)