This case highlights the intricate interactions in nature, between microbes, vectors and humans leading to zoonotic infection. Many other such relationships probably remain to be discovered as part of the One Health movement.

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1. Relman DA. Universal bacterial 16S rRNA amplification and sequencing. In: Persing DH, Smith TF, Tenover FC, White TJ, editors. *Diagnostic Molecular Microbiology: Principles and Applications*. Washington DC: ASM Press, 1993; 489–95.
2. Thao ML, Baumann P. Evidence for multiple acquisition of *Arsenophonus* by whitefly species (Sternorrhyncha: aleyrodidae). *Curr Microbiol* 2004; 48: 140–4.
3. Truskinovsky AM, Dick JD, Hutchins GM. Fatal infection after a bee sting. *Clin Infect Dis* 2001; 32: e36–8.
4. Edouard S, Subramanian G, Lefevre B, et al. Co-infection with *Arsenophonus nasoniae* and *Orientia tsutsugamushi* in a traveller. *Vector Borne Zoonotic Dis* 2013; 13: 565–71.
5. Darby AC, Choi JH, Wilkes T, et al. Characteristics of the genome of *Arsenophonus nasoniae*, son-killer bacterium of the wasp *Nasonia*. *Insect Mol Biol* 2010; 19 (Suppl 1): 75–89.
6. Ferree PM, Avery A, Azpurua J, Wilkes T, Werren JH. A bacterium targets maternally inherited centrosomes to kill males in *Nasonia*. *Curr Biol* 2008; 18: 1409–14.
7. Van Engelsdorp D, Evans JD, Saegerman C, et al. Colony collapse disorder: a descriptive study. *PLoS One* 2009; 4: e6481.
8. Snodgrass RE. *Anatomy and Physiology of the Honeybee*. New York: McGraw-Hill, 1925.

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Acute poisoning by dexmedetomidine-containing chewing gum in a child

To the Editor,

In this report, we describe an unusual case of acute poisoning caused by dexmedetomidine-adulterated chewing gum.

A 7-year-old boy was admitted to the Department of Pediatrics and Adolescent Medicine with loss of consciousness. The patient became unarousable shortly after consuming a piece of chewing gum in ordinary packaging. The chewing gum was retrieved from the patient's mouth and he was immediately sent to the hospital. On arrival to the Accident and Emergency department, his blood pressure was 119/76 mmHg, with pulse rate of 76 beats per minute and respiratory rate of 22 breaths per minute. He was unresponsive with a Glasgow Coma Score of 4/15 (E1V2M1). Pinpoint pupils were observed, so opioid overdose was initially suspected and naloxone was given. Initial laboratory investigations, including arterial blood gas, complete blood count, clotting profile, liver and renal functions, electrolytes, blood glucose and ammonia were all unremarkable. Ethanol level in the blood was undetectable. Computed tomography of the brain did not reveal any focal lesion or abnormality. The patient was admitted to the paediatrics intensive care unit (PICU) for close monitoring and endotracheal intubation was performed for airway protection. He gradually regained consciousness and was extubated on the following day. He recovered uneventfully and was discharged a week after admission. Further follow-up physical examination and brain imaging at 2 months after discharge showed absence of long-term sequelae.

Toxicology investigation was performed on the chewing gum remains and patient's urine specimen. The chewing gum was extracted by liquid-liquid extraction as follows: the specimen was first extracted with 70% acetonitrile (0.1 g/mL) and sonicated for 30 min. Supernatant was collected after centrifugation; 0.5 mL of the supernatant was mixed with 3.5 mL purified water and 50 µL of pinazepam (internal standard). The mixture was then extracted using De-tox Tube A by mechanical shaking for 30 min. After centrifugation, 1.25 mL of the upper organic phase was aspirated, dried under compressed air, and reconstituted in 0.8 mL 30% acetonitrile. The supernatant was injected onto the high performance liquid chromatograph (HPLC) followed by diode array detection (DAD). The same extract was also subjected to a separate tandem mass spectrometry (MS/MS) analysis for confirmation. The urine specimen was analysed by LC-MS/MS after 1:5 dilution with water. Dexmedetomidine was detected in both the chewing gum remains and the patient's urine specimen. Other drugs detected in the urine, including midazolam, naloxone and rocuronium, were all given after hospitalisation.

Dexmedetomidine is an alpha-2 adrenergic receptor agonist with sedative, anxiolytic, analgesic and cardiovascular stabilising effects. It is notable for its ability to achieve sedation without significant respiratory depression.¹ Dexmedetomidine was developed in the 1980s and approved by the Food and Drug Administration for human use in 1999. It has a distribution half-life of 6 minutes and plasma half-life of 2 hours.¹ Common uses include sedation in intensive care and for paediatric procedures, controlled

hypotension, locoregional analgesia, and as adjunct analgesia in surgeries to reduce morphine requirement. The recommended route of administration is intravenous and the usual dosage is 0.2–0.7 µg/kg/hr. Oral bioavailability is poor due to first-pass metabolism but sublingual bioavailability is high.¹ In Hong Kong, dexmedetomidine is a prescription-only medication and only available as injection or infusion solution. Recent studies show that intranasal administration of dexmedetomidine is effective and safe for sedation in paediatric patients. Dexmedetomidine is metabolised through N-glucuronidation and hydroxylation. Most inactive metabolites are excreted renally.¹ Common side effects include coma, dry mouth, hypotension, and bradycardia. Less common adverse effects include hypothermia, cardiac arrhythmias including AV block, pulmonary oedema and convulsions.¹ The pupils may be constricted or dilated.² In case of overdose, the management is supportive treatment for hypotension, bradycardia and other adverse effects. Maintaining a clear airway and ensuring adequate ventilation is important. The benefit of gastric decontamination is uncertain and no antidote is available.²

Dexmedetomidine identified in the patient's urine and the chewing gum was the sole agent that could explain the patient's clinical presentation. The presence of dexmedetomidine in chewing gum is highly unusual. The source of the chewing gum was a mystery. The patient lived and studied in Hong Kong but he travelled to mainland China a few times every year to visit his relatives. According to the patient, the chewing gum just 'appeared' in his bag during his last visit to mainland China (August 2019); presumably it was placed there by an unknown person. Although drug-facilitated crime was suspected, the actual intention remained undetermined.

Recently, dexmedetomidine-adulterated chewing gum has been reported as used in drug-facilitated sexual assault (DFSA) in Taiwan and China.³ This type of sedative chewing gum, packaged as ordinary Wrigley's Doublemint or Juicy Fruit chewing gum, can be purchased through the internet. According to the product description, the chewing gum can cause immediate decrease in consciousness upon consumption with effects lasting for 3–5 hours. Since this type of chewing gum is easily obtainable, it can be a potential threat to the general public.

Unlike health supplements and herbal medications, chewing gum is not a common source of drug adulteration. Publications on toxicity cases related to drug-adulterated chewing gum are even more scarce. Analyses on lifestyle products revealed sildenafil in a brand of chewing gum called

Super Lover, available on the internet.⁴ Stimulant ('energy') chewing gum containing caffeine has been reported to cause acute intoxication when consumed in substantial amounts.⁵

Dexmedetomidine-adulterated chewing gum is a rare cause of intoxication. To our knowledge, this is the first reported local case of toxicity due to dexmedetomidine-containing chewing gum in Hong Kong. To conclude, frontline clinicians and the general public should be aware that although uncommon, foods adulterated or spiked with drugs are worthy of consideration in cases of acute unconsciousness. High clinical suspicion and vigilance is thus required for case detection. In suspected cases, laboratory investigation of urine specimen, as well as the suspicious product, could help identify the culprit.

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1. Kaur M, Singh PM. Current role of dexmedetomidine in clinical anesthesia and intensive care. *Anesth Essays Res* 2011; 5: 128–33.
2. TOXBASE. Enquiry on dexmedetomidine. www.toxbase.org.
3. Pan M, Wang X, Zhao Y, et al. A retrospective analysis of data from forensic toxicology at the Academy of Forensic Science in 2017. *Forensic Sci Int* 2019; 298: 39–47.
4. Do TT, Theocharis G, Reich E. Simultaneous detection of three phosphodiesterase type 5 inhibitors and eight of their analogs in lifestyle products and screening for adulterants by high-performance thin-layer chromatography. *J AOAC Int* 2015; 98: 1226–33.
5. Natale F, Cirillo C, Di Marco GM, et al. When chewing gum is more than just a bad habit. *Lancet* 2009; 373: 1918.

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