

Are attempts to develop a non-lethal knock-out gas undermining the treaties that ban chemical weapons? Michael Brooks investigates

Gas attack



Police can use tear gas (left), but the legality of using a knock-out gas to end the 2002 Moscow theatre siege (right) is questionable

● AMONG the medical profession, anaesthetists have something of a reputation for being boring. While surgeons do the heroics, it's anaesthetists who put you to sleep, keep you ticking over and then wake you up again when the drama is over.

It seems hard to believe then that a group of them stand accused of derailing a 79-year-old global arms control treaty. The chemical weapons convention is under threat from attempts to turn anaesthetic agents into "non-lethal" chemical weapons, says the treaty watchdog, the Organisation for the Prohibition of Chemical Weapons (OPCW).

Drugs such as these, designed to knock people out quickly and without doing lasting harm, are touted by some as a humane way of dealing with terrorists or hostage-takers, for example. Opponents say they are inherently dangerous, however – a view that seems to be supported by their track record.

Whether the current research into such agents breaches the convention seems to fall into a legal grey area. But allowing it to continue unchecked would be a slippery slope to the treaty's downfall, the OPCW says in a soon to be published internal report seen by *New Scientist*. "One of the great achievements in arms control is the banning of poisons and germs," says Mark Wheelis of the Federation of American Scientists (FAS) working group on the control of chemical and biological weapons. "I would hate to see those gains reversed, but that's what the push is right now."

It was the horrific poison gas attacks of the first world war that led to the 1925 Geneva protocol banning the use of chemical weapons. In 1997 this was augmented by the chemical weapons convention, which widened the ban to the development, production and possession of such agents. There are now 182 countries signed up, with the OPCW in charge of policing the convention and destroying any weapons.



The one significant exemption to the convention is for domestic law enforcement. According to Article II.7 of the convention, police officers – but not the military – are allowed to use chemicals that rapidly produce "sensory irritation or disabling effects which disappear within a short time". In other words, riot control agents such as tear gas and pepper spray are allowed.

Efforts to create more sophisticated non-lethal chemical weapons have been ongoing for decades. In the 1960s scientists in the US and UK tried to develop suitable agents based on fentanyl, a potent anaesthetic, then newly discovered. These came to naught, however, as the drug turned out to be too dangerous to use in this way.

Today the only people who are openly working on such drugs are a group of Czech anaesthetists based at the Institute of Experimental Medicine and Charles University Hospital in Prague, and the University of Defence in Hradec Kralove. In research presented



“The death rate of 16 per cent in Moscow was more than twice that of first world war gas attacks”

at the European symposia on non-lethal weapons held in Ettlingen, Germany, in 2005 and again in May this year, they described some of the agents they have been using.

An important class are the fentanyl-derived drugs. Fentanyl is an opioid, one of a large class of compounds that has a range of effects on the body, including knocking you out, relieving pain, and altering mood, as well as reducing breathing and heart rates. Other important classes are the benzodiazepines (such as Valium), which reduce anxiety and induce sleep, and the alpha2-agonists, which also induce sleep. Another option is the anaesthetic (and recreational drug) ketamine. The Czech anaesthetists have tested combinations of these drugs on monkeys and human volunteers. Their preferred cocktail is the benzodiazepine midazolam (a staple of human anaesthesia), combined with the alpha2-agonist medetomidine and a low dose of ketamine. This, they say, produced something “very close to fully reversible immobilisation” with little or no effect on heart rate or breathing. Other combinations also produced reversible immobilisation, but had side effects such as marked changes in blood pressure, heart rate and respiration.

In a statement to *New Scientist*, the Czechs maintain they are investigating non-lethal chemical weapons in case agents like these are used by terrorists. “Our research has a strictly defensive character,” they say.

This is not the main focus of their conference papers, however. In the 2007 one,

for example, the researchers acknowledge their work could also be useful in the “production of new pharmacological non-lethal weapons”.

Not all are so gung-ho about this new form of law enforcement, however. An analysis published in 2003 by three members of the FAS called the lure of non-lethal chemical weapons a “siren’s song” – seductive but dangerous.

A big stumbling block is that people vary in their response to anaesthetics (as with any drug) because of differences in body weight and biochemistry. Given the same dose of anaesthetic, some people would hardly be affected, some would lose consciousness, and some would even be killed.

The FAS researchers developed a mathematical model showing that even with a drug regarded as very safe – one with a therapeutic index (the ratio of the lethal dose to the knock-out dose) of 1000 – a level guaranteed to incapacitate 99 per cent of people could kill 9 per cent (see Graph). And typical anaesthetics are by no means very safe. The drugs being used by the Czechs have therapeutic indices of between 5 and 10, and so could kill a higher percentage of people.

And that’s under ideal, laboratory conditions. In practice, the drugs would be used in an enclosed space such as a building, where they would disperse slowly and the dose someone received would vary depending on how close they were to the source.

Both these factors seem to have played

Attempts to free hostages by feeding an opiate into the air-conditioning system killed 129 of them

a role in the only confirmed case of such drugs being used outside the laboratory. At the Dubrovka Theatre siege in Moscow in 2002, around 40 Chechens took some 800 hostages, demanding an end to the Chechen war. After two-and-a-half days’ stalemate, Russian special forces pumped what they later disclosed was a fentanyl derivative into the building’s air-conditioning system. An hour later they stormed the building, killing the Chechens and hauling out the hostages.

But 129 of the hostages never woke up. Most of the deaths seem to have resulted from people stopping breathing, either as a direct result of the drug, from inhaling vomit, or from their tongue blocking their airway. A lack of medical staff on standby to give victims an antidote didn’t help.

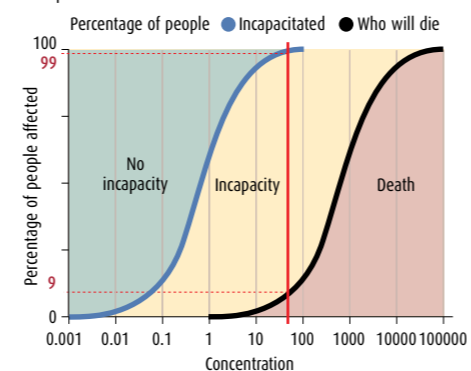
At 16 per cent, the death rate was more than twice that from the gas attacks of the first world war, as the FAS researchers pointed out. Of course, no one knows what the outcome would have been if the rescuers had relied on bullets and bombs, but the number of deaths suggests that “non-lethal” is a misnomer when applied to weapons like fentanyl.

Based on the Moscow siege as well as their own modelling, the FAS researchers concluded that “genuinely non-lethal chemical weapons are beyond the reach of current science”. This was a view echoed by the British Medical Association in a report entitled “The use of drugs as weapons”, published this year, in which it called on doctors to eschew research into such agents.

Yet even Wheelis, who was one of the FAS authors, feels you can never say never. He thinks that at some point it may be possible

LETHAL OR NOT?

A major problem with trying to design “non-lethal” chemical weapons based on anaesthetics is that people vary markedly in their physiological response to drugs. According to one model, the dose that would incapacitate 99 per cent of people would also kill 9 per cent of them



to design much more selective agents, thanks to our growing understanding of the brain’s biochemistry, including the receptor molecules that interact with anaesthetics. “If we knew the three-dimensional structure of all the different receptors and knew where they were and what kinds of [brain] circuits they affect, it seems plausible,” he says.

Trust drug

One option could be to design anaesthetics that affect consciousness without depressing breathing. Because drugs of this type could also be put to the more benign use of safer anaesthesia for surgery, research is ongoing. A strategy that has reached the stage of animal testing is to combine an opioid such as fentanyl with drugs that stimulate the part of the brain that controls breathing.

Whatever chemical cocktail is used, however, anyone who is knocked unconscious can suffocate if their tongue blocks their airway. Ensuring the airway is kept clear is just one of the crucial jobs that anaesthetists do during surgery.

An altogether different approach is to design new forms of non-lethal chemical weapons, such as ones that affect people’s emotions. “The ongoing revolution in the life sciences opens up the possibility of radical new forms of chemical incapacitants,” says Malcolm Dando, a neurobiologist and security expert at the University of Bradford in the UK.

Dando cites research into the hormone oxytocin, which has been shown to make people more trusting, and investigations of the brain’s fear circuits. “There will be people seeking these kinds of things, and there is a possibility they will succeed,” he says.

Just what kind of non-lethal chemical weapons research is going on is a mystery, however. Countries are under no obligation to declare their work because of the vagueness of the chemical weapons convention on non-lethal agents. “We just don’t have anything in detail about law enforcement chemicals,” says Ralf Trapp of the International Union of Pure and Applied Chemistry, who helped write the recent OPCW report.

The Czech work falls into a grey area because it is being carried out by civilians, albeit funded by the military. Obviously the Russians have been working on it, as demonstrated by the events in Moscow. Wheelis believes that under the convention, the legality of the Moscow incident was borderline: reports suggest both police and military forces took part, and while the

opponents were on Russian soil, the Chechen conflict is seen as a civil war by some. He finds it alarming that not one government called on the Russians to explain their actions, despite a clear entitlement to do so under the terms of the convention. Wheelis suspects this is because some countries have their own research programmes in this field that they are reluctant to jeopardise.

There are no publicly available reports of US research in this area, but the incapacitant approach seems to be in favour with some senior US officials. The Pentagon advisory Defense Science Board, for example, called for research into “calmative” weapons in a report published in 2004 titled “Future strategic strike forces”. The authors admitted that such research would have “significant” implications for the chemical weapons convention, but nevertheless called on the Pentagon’s Joint Non-Lethal Weapons Directorate to explore the options. At the 2005 non-lethal weapons conference in Germany, Michael Murphy, the US chair of a NATO committee set up to investigate non-lethal weapons, is reported to have spoken approvingly of the “Czech approach”, although he turned down



Both the Germans and the British used mustard gas in the first world war

New Scientist’s requests for an interview.

France is another country whose military may be interested in chemical incapacitants, according to the Sunshine Project, an international pressure group against biological and chemical weapons. The French navy’s medical research centre in Toulon, for example, maintains a behavioural pharmacology laboratory whose research has included investigations into the effects of a low dose of ketamine on human reaction times (*Neuroscience Letters*, vol 303, p 29). The Sunshine Project acknowledges that this research could be for benign purposes, but

asserts that because so little information about the research is available, it “could be interpreted as including illegal non-lethal chemical weapons activities”.

Against this background, the OPCW watchdog is adamant that the chemical weapons convention must be tightened up at the next five-yearly review meeting, to be held next April in the Netherlands. Its report calls on signatory countries to thrash out whether non-lethal chemical weapons are permitted in principle, and if so which types should be allowed, how they should be declared, and what the quantities and delivery systems should be. Whatever the outcome, the watchdog says it will need more resources for testing a new generation of non-lethal chemical weapons.

Will these demands be met? Similar calls made at the last review conference, in 2003, went unheeded; the agenda is set by the signatory countries, not the watchdog. In fact critics of the OPCW say it is in thrall to the US, its major funder.

If no action is taken, it looks as though non-lethal chemical weapons will emerge on the international scene by default. “They will continue to use them, and after a while, it

<http://technology.newscientist.com/channel/tech/weapons>