Corticosteroids, for example, can reduce the inflammation response. "Coming up with an effective treatment for chlorine is hugely challenging", points out Hay. "We all have chlorine regularly circulating in our blood, it slips in and out very easily". Chlorine is a highly corrosive chemical and can act with rapidity. Alternatively, as with mustard gas, there might be a latency period. Victims who do not appear to be in immediate distress might be overlooked by medical professionals.

"The solubility of the gas determines where the problem is going to be", said Hay. "Ammonia is very soluble, so the upper airways are affected, chlorine affects the middle airways, and phosgene, which is relatively insoluble, penetrates deep, so the alveoli are the focus of response." Over 300 000 tonnes of bromine are produced each year; manufacturing plants are considered by the US Department of Homeland Security to be high-risk targets for terrorist attacks. Inhalation of bromine can result in death; as things stand only standard supportive care is available to those exposed to it. There are countermeasures in development for both chlorine and mustard gas, although as of yet nothing is available for first-responders.

Atropine is an effective antidote for the nerve agents, but it has to be applied more or less straight away. This is not always feasible—victims of chemical attacks could take days to reach health-care facilities. The treatments for cyanide also require rapid deployment, as well as intravenous administration, which might be impossible during a large-scale attack. Test kits that can detect and identify chemical agents are routinely available to the military but are not distributed to civilian first-responders.

Research into toxic inhalation events is mostly funded by the NIH Countermeasures Against Chemical Threats (CounterACT) programme. This puts activities at the mercy of the vicissitudes of US Government policy. The ATS report draws attention to the prohibitive cost of obtaining approval from the US Food and Drug Administration for any new therapies to treat inhalation injuries. Moreover, because inhalation disasters are infrequent and unpredictable, it is difficult to attract interest from the pharmaceutical industry, meaning therapies are more or less orphan medicines. "We are at risk of these agents at all times, so it is important to put the resources into research and public health preparedness", stressed Summerhill.

The burgeoning field of green chemistry aims to find alternatives to toxic chemicals. "Chlorine is one of the chemicals that has been earmarked for replacement, but it is a problematic prospect because chlorine is so effective and ubiquitous", explained Hay. He adds that the chemical industry is well aware of the risks of their products. They have made it extremely difficult for non-state actors to get hold of chemicals that can be used as weapons, and have well established procedures for safe transportation. Hay suggests beginning discussions over whether the industry might also help fund prospective treatments for those agents that they mass produce—chlorine and bromine, for example. After all, the people most vulnerable to toxic inhalation injuries are the ones who work with dangerous chemicals.

Talha Khan Burki

The death of Mimì in Puccini's *La Bohème*: not an ordinary tubercular heroine

Operas can provide information about medical knowledge of the past, especially as conveyed by and to non-physicians. Among the diseases that opera characters suffered from, tuberculosis features rather frequently: Antonia in the *Tales of Hoffmann* (written in 1881 by Jacques Offenbach [1819–80]), Violetta in *La Traviata* (written in 1853 by Giuseppe Verdi [1813–1901]), and Mimì in *La Bohème* (written in 1896 by Giacomo Puccini [1858–1924]) are tragically doomed to die from tuberculosis. According to Hutcheon and Hutcheon, "as a disease that affects the lungs, and thus involves (literally and metaphorically) both inspiration and expiration, [tuberculosis] is also perhaps the archetypal operatic disease."

In particular, when Mimì comes on stage in act one of *La Bohème*, she provides the audience with precious details regarding the future course of her illness. Rodolfo, the Bohemian and penniless poet, is gazing through the window in his garret when he hears a timid knock at the door. It is Mimì, a lovely but frail neighbour, whose

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For more on **sleepwalking in Italian operas** see *Eur Neurol* 2010; **63:** 116–21

For more on **chronic cor pulmonale** see *Heart* 2003; **89:** 225–30

For more on **chronic cor pulmonale in pulmonary tuberculosis** see *Acta Med Scand* 1952; **142:** 315–24

For more on **Eleonora Duse** see Roma: Signorelli, 1938

candle has blown out. Breathless and cold ("Il respir… Quelle scale…" ["I'm out of breath… the stairs…"]), the girl turns pale and faints; the key and the candlestick fall from her hands. Rodolfo notices the beauty of her face and falls in love immediately. After regaining consciousness, Mimì wants to leave, but the candle has gone out again because of the wind and the room is dark. While pretending to look for the key he has already found, Rodolfo meets her hand and, surprised by its coldness, intonates the famous aria "Che gelida manina [*What a frozen little hand*]".

The cold limbs and the breathlessness might suggest that Mimì's pulmonary tuberculosis was complicated by chronic cor pulmonale. The term cor pulmonale refers to the structural changes and functional deterioration that occur in the right ventricle resulting from pulmonary hypertension, which is associated with various lung, upper airway, and chest wall diseases. The clinical signs of cor pulmonale displayed by Mimì include dyspnoea, coldness of the hands, and debilitation. As cor pulmonale is a frequent finding in cases of longstanding and widespread pulmonary tuberculosis, Mimì might have been in a late stage of the disease. Lung diseases complicated by cor pulmonale are generally associated with poor survival because, when the cardiac symptoms set in, the patient is already weak.

The frozen hand of the consumptive girl is not mentioned either in the original novel (*Scènes de la vie de Bohème* written in 1847–49 by Henri Murger [1822–61]) or in the play (*La vie de la Bohème* directed in 1849 by the young playwright Théodore Barrière [1823–77]) that inspired the opera. Therefore, this detail was introduced for the first time by the authors of the libretto: Giuseppe Giacosa (1847–1906) and Luigi Illica (1857–1919).

Giacosa was a dramatist of good repute, highly regarded for his warmth and wisdom. He was a collaborator and close friend of Eleonora Duse (1858–1924), one of the greatest Italian actresses of all time. In particular, Giacosa personally looked after Duse's health when she had tuberculosis. There is plenty of evidence that the Italian actress was in poor health, as stated in her biography, written by Olga Resnevič Signorelli (1883–1973): "On the eve of the performance, she was struck down by a violent hemoptysis. Her youth had fought the disease, but she suffered the consequences for the rest of her life." Giacosa commended Duse to the care of the Italian physician Carlo Forlanini (1847–1918), the inventor of artificial pneumothorax. Giacosa's acquaintance with tuberculosis, when he assisted Eleonora Duse, allowed him to reconstruct a precise outline of Mimì's condition. Hence, it is possible the reference to the "frozen little hand" in people suffering from tuberculosis complicated by chronic cor pulmonale derives from the personal knowledge of tuberculosis gained by the librettist.

This last detail confirms that 19th-century operas might provide us with valuable (and unexpected) information about medicine during that period, including on respiratory medicine and lung diseases. In particular, *La Bohème* by Puccini could contain an accurate description of symptoms of cor pulmonale chronicum in the same decades as illustrious pathologists such as Julius Cohnheim (1839–84) and William Osler (1849–1919) first described the effects of respiratory diseases on the right ventricle. The term cor pulmonale came into use only in the first 30 years of the 20th century.

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