

## Severe methaemoglobinaemia after flexible fibreoptic bronchoscopy

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**ABSTRACT** A patient with the acquired immunodeficiency syndrome (AIDS) developed severe cyanosis after bronchoscopy (oxygen saturation 34%) from methaemoglobinaemia. This was thought to be due to enhanced absorption of local anaesthetic from the nasopharynx or trachea as a result of candidiasis. The patient responded dramatically to intravenous methylene blue.

Severe cyanosis during or after bronchoscopy usually results from hypoxaemia from pneumothorax, pulmonary haemorrhage, or bronchoconstriction. We report a patient with the acquired immunodeficiency syndrome who developed cyanosis as a result of methaemoglobinaemia immediately after bronchoscopy. This was probably due to systemic absorption of the topical anaesthetic used to anaesthetise the nasopharynx (benzocaine) or the trachea (lignocaine).

### Case report

A 30 year old man with the acquired immunodeficiency syndrome (AIDS) and chronic oropharyngeal candidiasis underwent bronchoscopy to evaluate new nodular densities on the chest radiograph. He denied recent use of amyl nitrite or other drugs. The nose and nasopharynx were anaesthetised with several sprays of Cetacaine topical anaesthetic (benzocaine 14% and tetracaine 2%). About 10 ml of a 2% solution of lignocaine (lidocaine USP) was given through the bronchoscope to anaesthetise the larynx and major airways. Multiple transbronchial biopsy specimens were obtained and bronchoalveolar lavage was performed without difficulty.

Immediately after bronchoscopy the patient became profoundly cyanosed. A chest radiograph showed no new infiltrate or pneumothorax. An arterial blood sample, obtained while the patient breathed ambient air, was chocolate brown in colour. The pH was 7.36, the arterial oxygen tension ( $P_{aO_2}$ ) 11.2 kPa and the arterial carbon dioxide tension ( $P_{aCO_2}$ ) 5.9 kPa. Oximetry disclosed an arterial oxygen saturation of 34%. Spectrophotometric analysis of the blood sample indicated that 72% of the circulating haemoglobin was methaemoglobin.

Initially the patient appeared quite ill, but he responded

dramatically to 50 mg of methylene blue given intravenously. Transbronchial biopsy specimens showed non-specific inflammatory changes only and cultures of bronchial secretions were negative. The patient was discharged the following day with an arterial oxygen saturation of 98%.

### Discussion

Our patient developed profound cyanosis immediately after bronchoscopy. An intrathoracic catastrophe was suspected at first but the chocolate brown colour of the arterial blood sample led to a diagnosis of methaemoglobinaemia. The cyanosis resolved after intravenous administration of methylene blue.

In normal individuals a small amount of the haemoglobin in red blood cells is spontaneously oxidised to methaemoglobin each day. Methaemoglobin is reconverted to haemoglobin, however, by the action of the enzyme NADH methaemoglobin reductase, so the concentration of methaemoglobin remains below 2%. A shift in this equilibrium towards methaemoglobin may be inherited or acquired. Hereditary methaemoglobinaemia is caused by a homozygous deficiency of NADH-methaemoglobin reductase or by the presence of a variant haemoglobin such as haemoglobin M.<sup>1,2</sup> The acquired form of methaemoglobinaemia results from exposure to an appropriate oxidising agent in sufficient quantities to overwhelm the metabolic processes that reconvert methaemoglobin to haemoglobin.<sup>1</sup> Although cyanosis is often detectable when methaemoglobin is present in concentrations as low as 1.5-2.0 g/dl, most episodes of methaemoglobinaemia are asymptomatic and do not require specific treatment; indeed, the condition is rarely symptomatic unless the concentration of methaemoglobin exceeds 20%. As the concentration approaches 60-70%, fatigue progresses to coma and death.<sup>9,10</sup> Severe methaemoglobinaemia is rapidly reversed by the intravenous administration of the reducing agent methylene blue (1-2 mg/kg in a 1% solution over five minutes).<sup>5,11</sup>

The normal colour and the oxygen saturation of arterial blood from our patient before and after the acute episode of cyanosis excluded the possibility of hereditary methaemoglobinaemia and suggested that the disorder was acquired at the time of the bronchoscopy. Acquired methaemoglobinaemia has been associated with several topical anaesthetic drugs that contain an aniline ring or are metabolised to compounds that contain aniline like structures.<sup>3</sup> Of the three anaesthetics our patient received (lignocaine, benzocaine, and tetracaine), tetracaine is least likely to have caused methaemoglobinaemia as neither the parent compound nor its major metabolite (*p*-aminobenzoic acid) contains an aniline ring.<sup>4</sup>

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Lignocaine occasionally causes methaemoglobinaemia in patients who are unusually susceptible to the disorder.<sup>5</sup> The mechanism of increased susceptibility is not always clear. A heterozygous form of NADH-methaemoglobin reductase deficiency is probably the most common cause. We were not able to measure the enzyme in our patient. Increased susceptibility to methaemoglobinaemia seems unlikely in that he could recall no previous episode of cyanosis despite prior injection of the drug for dental work and the suturing of skin lacerations.

Benzocaine is known to cause a dose related methaemoglobinaemia in normal individuals after parenteral administration or ingestion.<sup>4</sup> The drug is widely used topically and in suppositories because it is minimally absorbed from intact skin or mucous membranes. Therapeutic doses of benzocaine have caused severe methaemoglobinaemia when systemic absorption across the stomach or rectum has been enhanced by the presence of gastritis or rectal fissures<sup>5-7</sup> and even, occasionally, when the absorbing surface appeared normal.<sup>3</sup> Excessive quantities of benzocaine were not used in this case. We suspect that *Candida* infection in this patient's oropharynx disrupted the mucosal surface sufficiently to cause excessive systemic absorption of the benzocaine and resulted in a dose related methaemoglobinaemia.

We have found reports of two patients who developed methaemoglobinaemia after topical administration of an anaesthetic in the airways. Olson and McEvroy<sup>3</sup> and O'Donahue *et al*<sup>8</sup> reported a patient who developed methaemoglobinaemia after receiving Cetacaine spray and benzocaine ointment for translaryngeal intubation. The patient recovered after treatment with methylene blue but methaemoglobinaemia recurred when topical benzocaine and lignocaine were used again the following day. Sandza *et al* described a patient who developed methaemoglobinaemia after the use of Cetacaine spray to anaesthetise the upper airways for fiberoptic bronchoscopy; this patient also recovered after administration of methylene blue.<sup>9</sup>

When severe cyanosis occurs during or immediately after

fiberoptic bronchoscopy, the possibility of methaemoglobinaemia as a complication of topical anaesthesia should be considered. To reduce the likelihood of this unusual complication of bronchoscopy in patients with oral candidiasis or other conditions that cause disruption of the oropharyngeal mucosa, we believe that the use of benzocaine should be abandoned in favour of lignocaine as increased systemic absorption of lignocaine across a damaged mucosa should not cause methaemoglobinaemia except in susceptible individuals.

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