



A rare case of anaphylaxis with intravesical administration of methylene blue dye during caesarean section

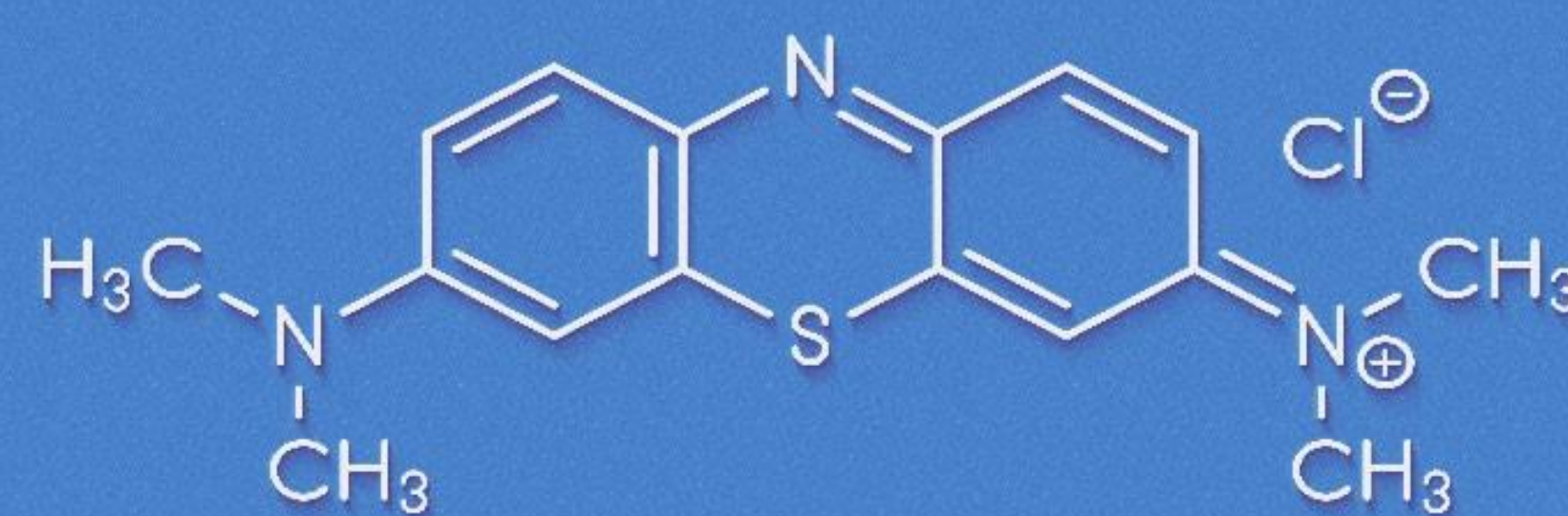
Dr Max Coupe-King, ST 7 Anaesthetist
Dr Aidan Melia, Consultant Anaesthetist

Background

- Blue dyes are increasingly used to investigate potential bladder injury during caesarean section.
- Rate of bladder injury during caesarean section is between 0.2% and 0.9%
- They are also a potential cause for perioperative anaphylaxis.
- The incidence of anaphylaxis in obstetric patients undergoing caesarean section is significantly lower than in non-obstetric adult cases, with the NAP6 survey identifying eight patients out of 233,866 obstetric anaesthetics per year, giving an incidence of 3.4 per 100,000 cases compared to 1:10,000 in the general adult population.¹
- Diagnosis and treatment of anaphylaxis during caesarean section is often delayed.

Blue Dyes

- Blue dyes are the 5th most common cause of perioperative anaphylaxis.
- However, all the cases of blue dye anaphylaxis noted in Nap 6 were related to Patent Blue dye.
- Despite its widespread use in medicine, anaphylaxis resulting from methylene blue has been rarely reported.²
- A literature review yielded only 6 cases of perioperative anaphylaxis to methylene blue and none of these were in awake patients or obstetric population.³
- Of interest, Methylene blue is a competitive inhibitor of guanylate cyclase and interferes with the vasodilatory actions of nitric oxide. It has been proposed (and used) as a treatment option for refractory anaphylaxis.



methylene blue

Case

ANTENATAL:

- A 35-year-old G5P2 woman presented to the maternity unit for induction of labour at 37 weeks due to prolonged premature rupture of membranes.
- This was an IVF pregnancy.
- She had undergone 2 previous caesarean sections for failure to progress in labour and had a laparoscopy and dye procedure 5 years previously.
- PMH: Contact dermatitis to nitrile blue gloves but no other known allergies.

LABOUR WARD:

- 12:00: An ARM was performed and an oxytocin infusion commenced as well as antibiotics for PPROM.
- 15:12 a sustained foetal bradycardia was noted on CTG and a category 1 caesarean section was declared.

THEATRE

- 15:20: A spinal anaesthetic was performed using alcohol/chlorhexidine 0.5% to prep the skin. 2.5ml of 0.5% heavy bupivacaine and 300mcg diamorphine were injected with no complications and a 100mcg/ml phenylephrine infusion was commenced at 20ml/hr alongside warmed Hartmann's. A satisfactory block was achieved.
- The bladder was catheterised with the aid of instillagel.
- 15:25: Skin prepped with chlorhexidine. Co-amoxiclav administered.
- 15:32: Live male infant delivered promptly in good condition.
- 15:58: During routine closure the obstetric team were concerned about possible risk of bladder injury due to the presence of adhesions and proximity of bladder to incision line.
- 16:10: 10mg of methylene blue was diluted in 1 litre of 0.9% saline and 300 ml introduced into her bladder via urinary catheter.
- This was announced by the obstetrician to the anaesthetist. No leak noted.
- 16:11: Patient complained of feeling unwell, heavy, tight chested, and short of breath.
- 16:11: Suspected anaphylaxis declared to theatre team by anaesthetist.
- 16:12: 500mcg adrenaline delivered IM to thigh. Methylene blue drained.
- 16:14: Salbutamol nebuliser administered. bladder washed out with saline.
- 16: 20: Hypotension noted and two 25mcg IV boluses of adrenaline given.
- 16:25: Second dose of 500mcg IM adrenaline to deltoid. Hypotension resolved.
- 16:39: Further episode of hypotension 82/57. Further 50mcg IV adrenaline given.
- 16:45: Stability achieved.
- 200mg IV hydrocortisone and 10mg IV Chlorphenamine given.
- 2500ml IV crystalloid administered in total.
- Phenylephrine infusion continued throughout and weaned before leaving theatre.
- A urologist attended and inserted a 3-way catheter with warmed saline running to irrigate the bladder overnight.
- No airway intervention was required beyond delivery of salbutamol nebulised in oxygen, there was no desaturation, tachycardia or any rash observed.



RECOVERY

- Patient was kept under close observation overnight, mast cell tryptases were sent, and she was discharged home 2 days later with a working diagnosis of allergy to methylene blue.
- Referral was made to a tertiary anaesthetic allergy clinic

Allergy Clinic

- 3 X mast cell tryptases taken immediately, at 4 hours later and the following day were all normal.

Skin Prick Testing

Substance	flare size (mm)
Histamine	20
Saline	Small red mark
Chlorhexidine	2
Latex	Small red mark
Fentanyl	Small red mark
methylene blue	Small red mark

Intradermal testing

Saline	4 mm	
Fentanyl	10 mm	
Chlorhexidine	12mm	
Methylene blue		

- The proximity of administration to the clinical presentation alongside the positive intradermal test strongly implicate Methylene Blue as the culprit agent.
- We propose she was sensitised to methylene blue during her chromopertubation procedure in 2018.
- The patient has been formally labelled as having a Methylene Blue allergy.

Reflections

- Although rare, it is important to remember that methylene blue can be a cause of anaphylaxis.
- Clear communication by theatre teams around administration of blue dyes can lead to rapid diagnosis and management of anaphylaxis.
- Mast cell tryptase values can be normal in anaphylaxis.⁴
- Allergy clinic is an important part of the patient's anaphylaxis journey.

References

- Anaesthesia, surgery, and life-threatening allergic reactions: protocol and methods of the 6th National Audit Project (NAP6) of the Royal College of Anaesthetists, Cook, T.M. et al., British Journal of Anaesthesia, Volume 121, Issue 1, 124 – 133
- Severe anaphylactic shock due to methylene blue dye , Wahid F.N et al, Journal of paediatric Surgery Case Reports 2 (2014), 117-118.
- Allergy like reactions to methylene blue following laparoscopic chromopertubation: A systematic review of the literature, European Journal of Obstetrics and Gynaecology and reproductive biology 238 (2019) 58-62
- Anaesthesia-related anaphylaxis: investigation and follow-up, Alex TD Mills, Paul JA Sice, Sarah M Ford, *Continuing Education in Anaesthesia Critical Care & Pain*, Volume 14, Issue 2, April 2014, Pages 57–62