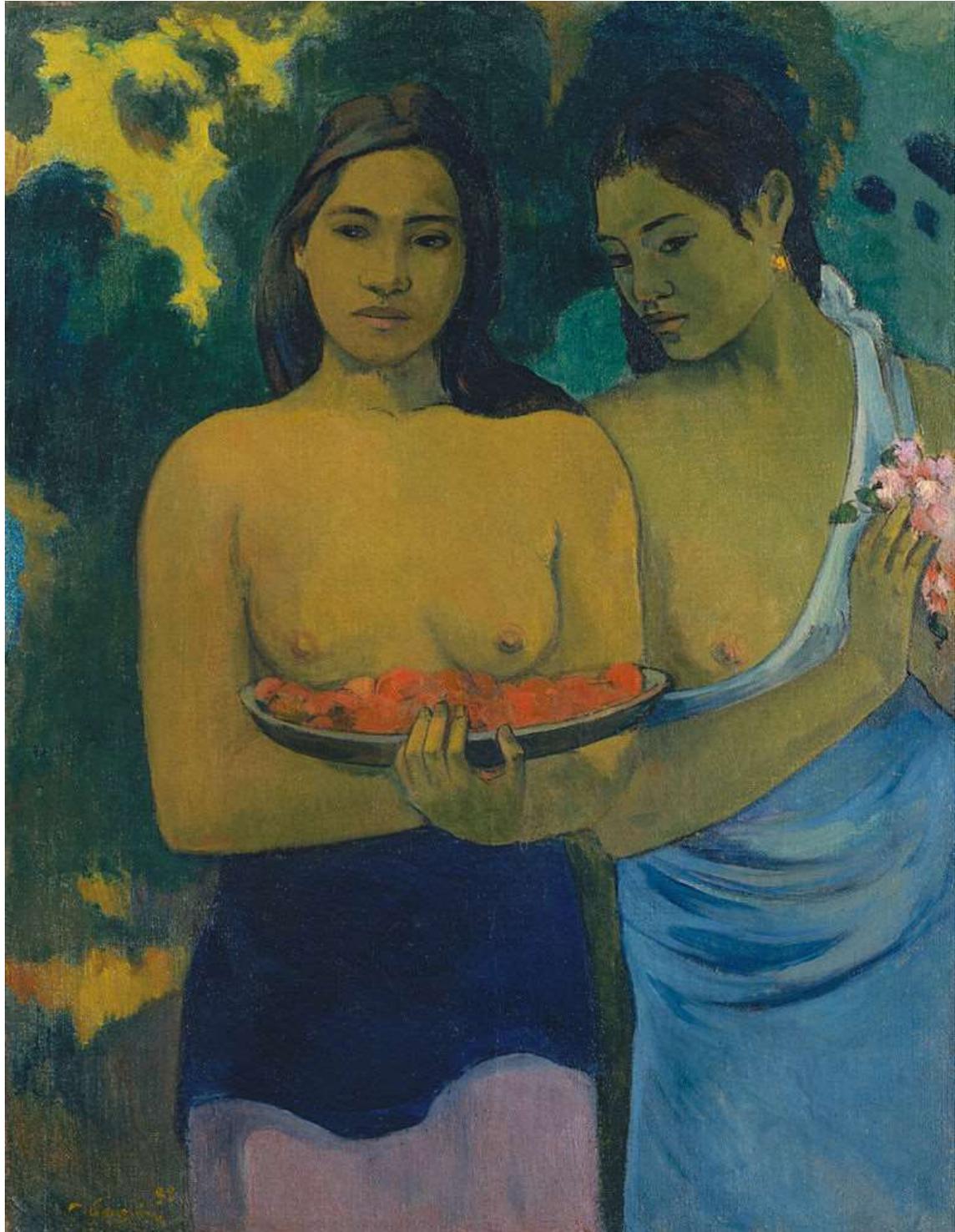


PROPOFOL RELATED INFUSION SYNDROME (PRIS)



"Two Tahitian Women", oil on canvas, 1889, Paul Gauguin.

“...I have to admit that it was nigh impossible to keep 400 young Frenchmen at work, sailors who had not seen a woman for six months, in view of what followed. In spite of all precautions, a young Tahitian girl slipped aboard and placed herself on the quarterdeck immediately above one of the big hatchways, which was fully open to allow air in to the sailors sweating at the capstan below. The young girl casually let slip the only piece of cloth which covered her, and appeared to the eyes of all the crew exactly as naked Venus appeared to the Phrygian shepherd. Truly, she had the celestial form of the goddess of Love. More and more sailors and soldiers crowded to the foot of the hatchway, and no capstan was ever wound with such alacrity as on this occasion. Only naval discipline succeeded in keeping these bewitched fellows from rioting; and indeed we officers had some little difficulty in restraining ourselves....”

Louis-Antoine, Comte de Bougainville, “Voyage Autour du Monde”, April 1768.

Of all the exotic lands that James Cook and Joseph Banks encountered during the Endeavour’s great and historic voyage of 1768-1771, none where perhaps as eagerly looked forward to by their crew than the fabled Pacific island of Tahiti. Earlier French reports had described a tropical paradise, an untouched Garden of Eden where the women walked around virtually naked and were all too happy to bestow their favors. The Endeavour carried large supplies of nails, not only for critical ship repairs but also as a currency of trade with the natives. The Tahitians had no need of silver or even gold, but they did value iron very much. Banks was much annoyed by the constant pilfering of their nails at the hand of the natives, writing in his journal...

“I do not know by what accident I have so long omitted to mention how much these people are given to thieving. I will make up for my neglect however today by saying that great and small Chiefs and common men all are firmly of the opinion that if they can once get possession of anything it immediately becomes their own”.

Banks’ outrage has perhaps been most eloquently answered by his biographer Patrick O’Brian...

“...In any case the thefts were not all on the one side: Captain Wallis had taken possession of the entire island of Tahiti and its dependencies, which brings to mind the remark about the relative guilt of the man who steals a goose off a common and the other who steals the common from under the goose!”.

Try as much as he could however, Banks had a devil of a time hanging on to the ships nails, due to the constant pilfering by his own crew. In June 1769 a crisis was reached when a hundredweight bag of nails went missing. He recorded...

“One of the thieves was detected but only 7 nails were found upon him out of 100 Wht and he bore his punishment without impeaching any of his accomplices. This loss is of a very serious nature as these nails if circulated by the people among the Indians will much lessen the value of Iron, our staple commodity”.

Banks valued the nails as means of trade with the natives for important supplies and natural history specimens, and so did his crew value the nails, though for an altogether different reason. In his magisterial "Age of Wonder", Richard Holmes, explains why...

"Among the able seamen the initial going rate was one ship's nail for one ordinary fuck. But hyperinflation soon set in. The Tahitians well understood a market economy. There was a run on anything metal that could be smuggled off the ship - cutlery, cleats, handles, cooking utensils, spare tools, but especially nails. It was said that the Endeavour's carpenter soon operated an illegal monopoly on metal goods, and nails were leaving the ship by the sackful".

Banks pointed out the trade to Cook, who was outraged. He immediately made great efforts to put a stop to the practice of sexual bartering, "quite unsupported", he later drily observed, even among his own officers. He did manage to remain philosophical, however, and in an attempt to dissuade his crew from the illicit "trade" related to them, not without a sense of humor, the fate of Captain Wallis's ship, the Dolphin, that had left Tahiti two years previously. So many nails had been surreptitiously extracted from her timbers that upon the first storm at sea they encountered the ship near fell apart!

Captain James Cook's alarming tale of the near fate of the Dolphin at sea, rather refutes the old wisdom that "one cannot have too much of a good thing". The crews of ships that landed in Tahiti in the Eighteenth century, thought all their Christmases had very much come at the one time - there was certainly no holding back on a very good thing!...until perhaps such time as Cook explained to them the possible consequences once back on the high seas!

When we require our patients to be mechanically ventilated, we have at our disposal a very very good thing, in the form of the propofol infusion which allows them to tolerate what is to many a terrifying experience. While propofol is a good thing in the short term, we need take cautionary note of the tale of HMS Dolphin - it is indeed possible to have too much of a good thing!

PROPOFOL RELATED INFUSION SYNDROME (PRIS)

Introduction

Propofol Related Infusion Syndrome (PRIS) is a rare but **life-threatening** condition characterized by:

Acute refractory bradycardia (which can progress to asystole) and one or more of:

- Metabolic acidosis
- Rhabdomyolysis
- Hyperlipidaemia
- Enlarged or fatty liver

Its etiology is poorly understood.

It is often fatal.

It usually only effects patients undergoing longer term treatment with high doses of propofol.

The index of suspicion should remain high, especially in cases of patients who have been on prolonged and high dose infusions, and who develop cardiovascular instability.

Mechanism

The exact mechanism of PRIS is poorly/ not understood.

Theories include:

- Direct mitochondrial respiratory chain inhibition
- Impaired mitochondrial fatty acid metabolism

Risk Factors

Risk factors for the development of PRIS include:

1. High dose and prolonged infusions:
 - In general > **4mg / kg / hr for 48 hours**
 - However it may on occasions develop at lower doses

2. Younger age groups
3. Acute neurological injury
4. Low carbohydrate intake:
 - Low carbohydrate supply is a risk factor for PRIS because energy demand is satisfied by lipolysis if carbohydrate supply is low.
5. Possibly in association with other agents:
 - Catecholamine infusion
 - Corticosteroids infusion

Clinical features

Suspicion should be high for patients who are on propofol infusions, (especially if high dose and for prolonged periods), and who develop:

1. The need for increasing inotrope support
2. Cardiovascular collapse:
 - Particularly bradycardia with refractory hypotension
 - May be reflected in PICCO, PAC, ECHO
3. Urine may show myoglobinuria.

Investigations

Blood tests:

1. U&Es:
 - Renal impairment/ failure
2. Rhabdomyolysis (high CK / hyperkalaemia)
3. ABGs/ VBGs/ lactate:
 - Unexplained lactic acidosis
4. Lipaemic serum
5. LFTs:

- Elevated liver enzymes
6. Propofol levels (if available)

ECG:

ECG changes can include:

- RBBB
- Bradycardia/ Arrhythmia
- Heart block
- Brugada like ECG (coved type, i.e convex-curved ST elevation in V1-V3)

Management

The index of suspicion should remain high, especially in cases of patients who have been on prolonged and high dose infusions, and who develop cardiovascular instability.

Early warning signs should be monitored for (rising lactate, CK, urinary myoglobin, characteristic ECG changes).

If the condition is suspected:

1. **Cease the propofol infusion immediately.**
2. Supportive care:
 - Inotropes (can be resistant)
 - Consider pacing (can be resistant)
 - ECMO (case reports, but reasonable given readily reversible pathology)
3. Dietary support:
 - Adequate carbohydrate intake (6-8mg/kg/min)
 - Carnitine supplementation (has some theoretical benefit)
4. Hemodialysis and haemoperfusion:
 - Has been used with success in some case reports
 - Eliminates propofol and its potentially toxic metabolites.



“HMS Resolution and Adventure in Matavai Bay, Tahiti” oil on canvas, 1776 William Hodges

References

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2 September 2015.