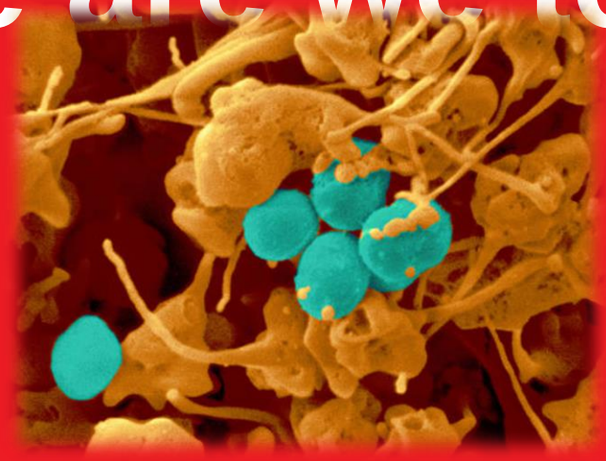
Bacterial Contamination of Platelets: Where are we today?



Blood Matters Conference
Halifax, Nova Scotia
Nov 16, 2018

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Canadian Blood Services

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Disclosures

- I am on the bioMérieux Scientific Advisory Committee

Learning objectives

1. What is the relationship between implementation of a different culture protocol and extension to a 7 day storage time (August 2017)
2. Why are we receiving more reports of possible bacterial contamination in our blood bank
3. Why are some bacteria still being missed, and does this matter
4. What has the impact of the new protocol been on the safety and adequacy of the platelet supply

Measures taken to reduce bacterial septic reactions before August 2017

- Validated, optimal skin disinfection (chlorhexidine and isopropyl alcohol)
- Diversion pouch for whole blood and apheresis kits
- Bacterial culture of all platelet components
  - BacT/ALERT aerobic bottle
  - 8 - 10 ml sample of buffy coat pool or apheresis collection
  - ≥ 24 hours post-collection
  - No post-inoculation hold
- Five day product storage

Assessment of efficacy

- 10 ml aerobic and 10 ml anaerobic cultures of ~ 1% of platelet production at outdate (QC cultures)
- Components with unusual appearance removed from inventory and cultured
- Reports of septic reactions from hospitals
  - Ideal investigation requires culture of residual component and patient

Residual risk of septic reactions and positive QC cultures Jan 2010 – Dec 2016

- CBS
  Non-fatal reactions: 5/555,000 1/111,000 **Fatalities:** 1/555,000 1.8/1,000,000
- Clinically significant organisms on QC culture: 6 – 7/10,000
- UK (2011 – Dec 31, 2014, 7 day platelet storage)
  Non-fatal reactions: ~1/1,000,000 **Fatalities:** 0
  3 near misses (abnormal appearance)

S. Ramirez-Arcos
Transfusion 2017;57:2177

Inventory challenges, 5 day shelf-life

- We do not accept hospital returns
- High overall system outdate for platelets (>25%)
- Inventory shortages, especially around 3 day weekend and holidays
- Both buffy coat and apheresis (TRIMA) products licensed for 7 day storage

Can we maintain or enhance bacterial safety and prolong platelet shelf-life to 7 days

Safeguard

Engage

Improve

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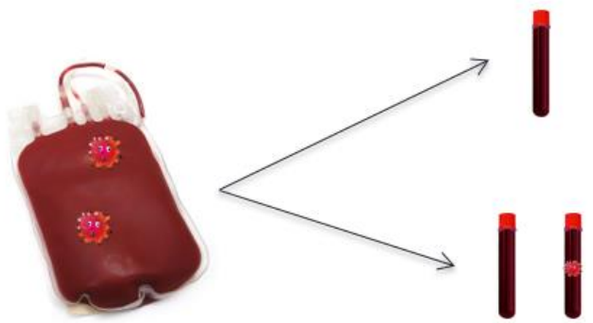
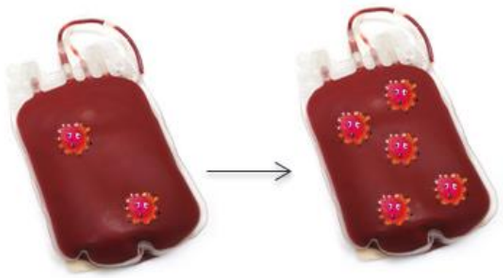
Sampling error is reduced by



Increasing volume of sample



Increasing delay before culture

Enhancements to culture protocol

- Increase time from collection to sampling
- Increase volume of product sampled
- Add anaerobic culture bottle, both to increase volume sampled (1 aerobic and 1 anaerobic bottle, each 8 ml of product) and to detect anaerobes
- Introduce a post-inoculation hold before placing products in inventory

New culture protocol and storage time

	March 2004- August 2017 (5 day storage)	Since August 2017 (7 day storage)
Sampling time post-collection (hours)	24 -30	≥ 36 h
Volume	8-10 ml	16-20 ml (40 ml for double apheresis)
Bottles	Only aerobic	Aerobic and anaerobic (both incubated for 7 days)*
Post-sampling quarantine	None	≥ 6 h

* Only for double apheresis collections: 3 aerobic bottles, 1 anaerobic bottle

Expected results post-implementation

- Initial positive rate – will increase both because sensitivity is improved (↑ true positive rate) and because of the addition of an anaerobic bottle (↑ false positive rate, particularly due to machine error)
- QC at expiration rates – should decrease, since fewer contaminated units missed on initial culture
- Septic transfusion reactions – should decrease
- Longer observation period necessary for rare events (septic reactions) or small denominator (QC cultures) to compare with historic data

Results, Routine cultures

	Jan 2010 – Dec 2016 (5d PLT)		Aug 2017 – Aug 2018 (7d PLT)	
	Buffy coat	Apheresis	Buffy coat	Apheresis
Number	601,988	186,737	98,391	15,826 doubles + 1,978 singles (17,804 collections/33,630 doses)
Initial positives (%)	390 (0.06)	269 (0.14)	291 (0.30)	151 (0.84)
Confirmed positives (%)	57 (0.01)	18 (0.01)	80 (0.08)	4 (0.02)
Strict anaerobes	NA	NA	58 (0.06)	2 (0.01)
Others	57 (0.01)	18 (0.01)	22 (0.02)	2 (0.01)
False positives (%)	228 (0.04)	206 (0.11)	104(0.11)	104 (0.66)

- Overall bacterial detection has increased ~ 8.0-fold (BC) and ~2.0-fold (APH). Mostly anaerobes
- Detection or aerobes and facultative anaerobes has increased ~2.0-fold (BC) and remained similar for APH
- False positive results have increased ~ 2.8-fold (BC) and ~ 6.6-fold (APH). Mostly anaerobes
- Since March 5, 2018: releasing associated components

Confirmed positives, Buffy coat pools

anaerobes

Species	N	Mean time to detection	Positive bottle(s)
Cutibacterium acnes (formerly *P. acnes*)*	51	110 ± 24	45 BPN, 1 both
Diptheroid bacillus*	2	117.1	2 BPN
*Staphylococcus saccharolyticus**	4	43 ± 16	8 BPN
Eggerthella lenta (formerly *Eubacterium lentum*)	1	40	BPN
Coagulase negative staphylococci	16	22 ± 13	4 BPA, 4 both
Staphylococcus aureus	2	13± 4	1 BPN, 1 both
Streptococcus groups C or G	3	8 ± 1.7	Both
Streptococcus agalactiae	1	11	Both

BPN = anaerobic bottle, BPA = aerobic bottle

* 28 out of the 80 confirmed positives (35%) involved culture of associated RBCs

Confirmed positive, Apheresis platelets

Platelet Type	Positive bottles	Time to Detection (hrs)	Species
Double	both	7.2	*Streptococcus viridans*
Single	BPN	51.4	Coagulase negative *Staphylococcus*
Double	BPN	79.4	*Diphteroid* bacillus
Single	BPN	83.5	*Propionibacterium acnes*

anaerobes

What is the value of the post-inoculation 6 hour quarantine?

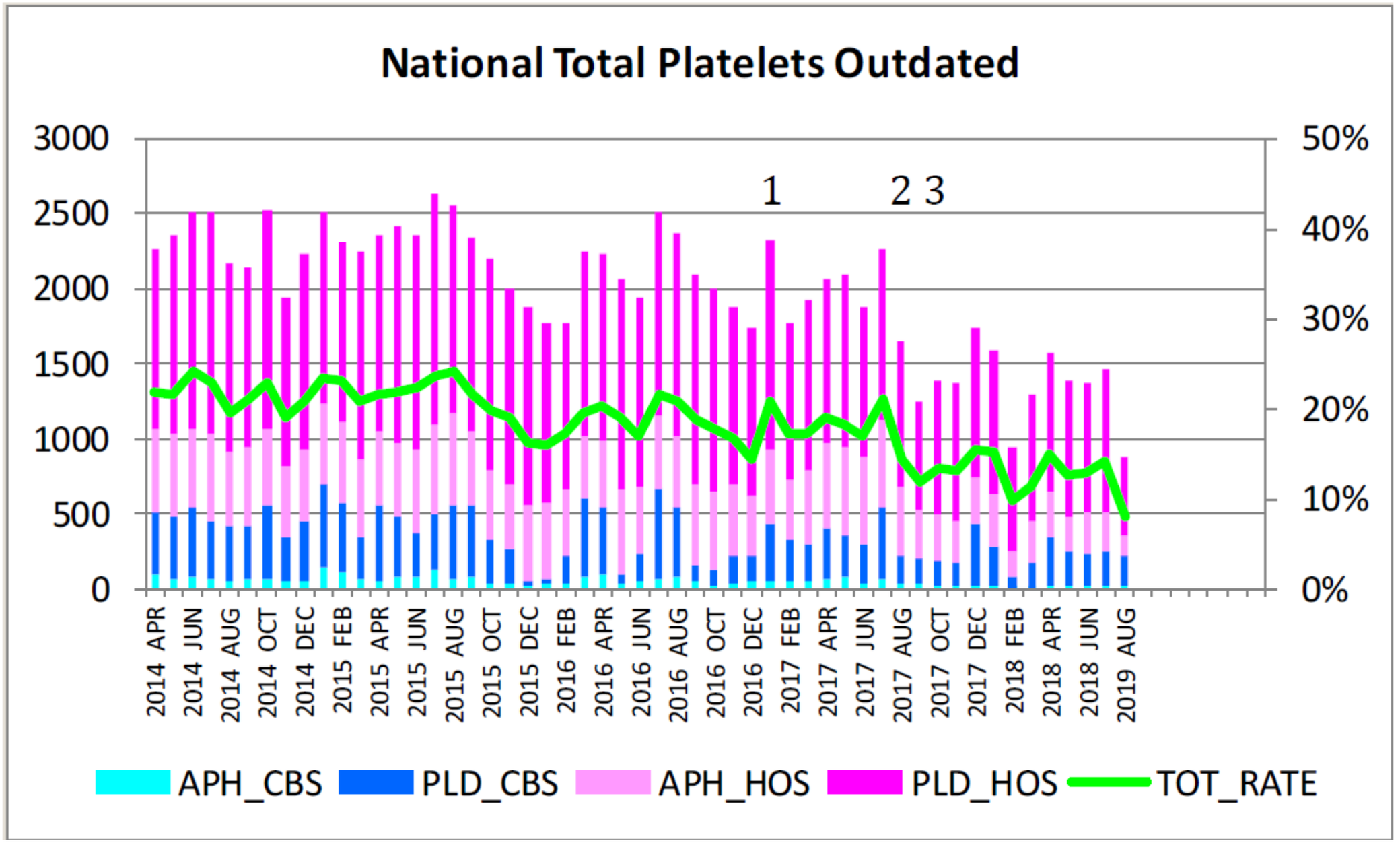
PC	Species	Bottle(s)	Detection time (hrs)
Apheresis (double)	*Streptococcus viridans*	2 BPA	7.2
		2 BPN	7.2
Pool	Haemolytic *Streptococcus* group G	BPA	9.36
		BPN	8.4
Pool	Haemolytic *Streptococcus* group G	BPN	6
		BPA	6.24

Residual risk – False negative screening results

	Platelets	Jan 2010 – Dec 2016 (5 days)	Aug 2017 – Aug 2018 (7 days)
QC sterility testing – Detection of contaminated units at expiry	Buffy coat pools	1/1,219	2/1,248[a]
	Apheresis units	1/1,062	0/1,079
Septic transfusion reactions		~1/100,000	~1/100,450[b] (Aug-Jul 2018)

[a] *Staphylococcus epidermidis*

[b] Non-fatal reaction involving a 7-day old platelet pool contaminated with *S. epidermidis*



1. Jan 2017 – Stakeholder Consultation: 2 Day Session
2. Aug 2017 – Extended Shelf Life
3. Sept 2017 – Apheresis Collections Reductions

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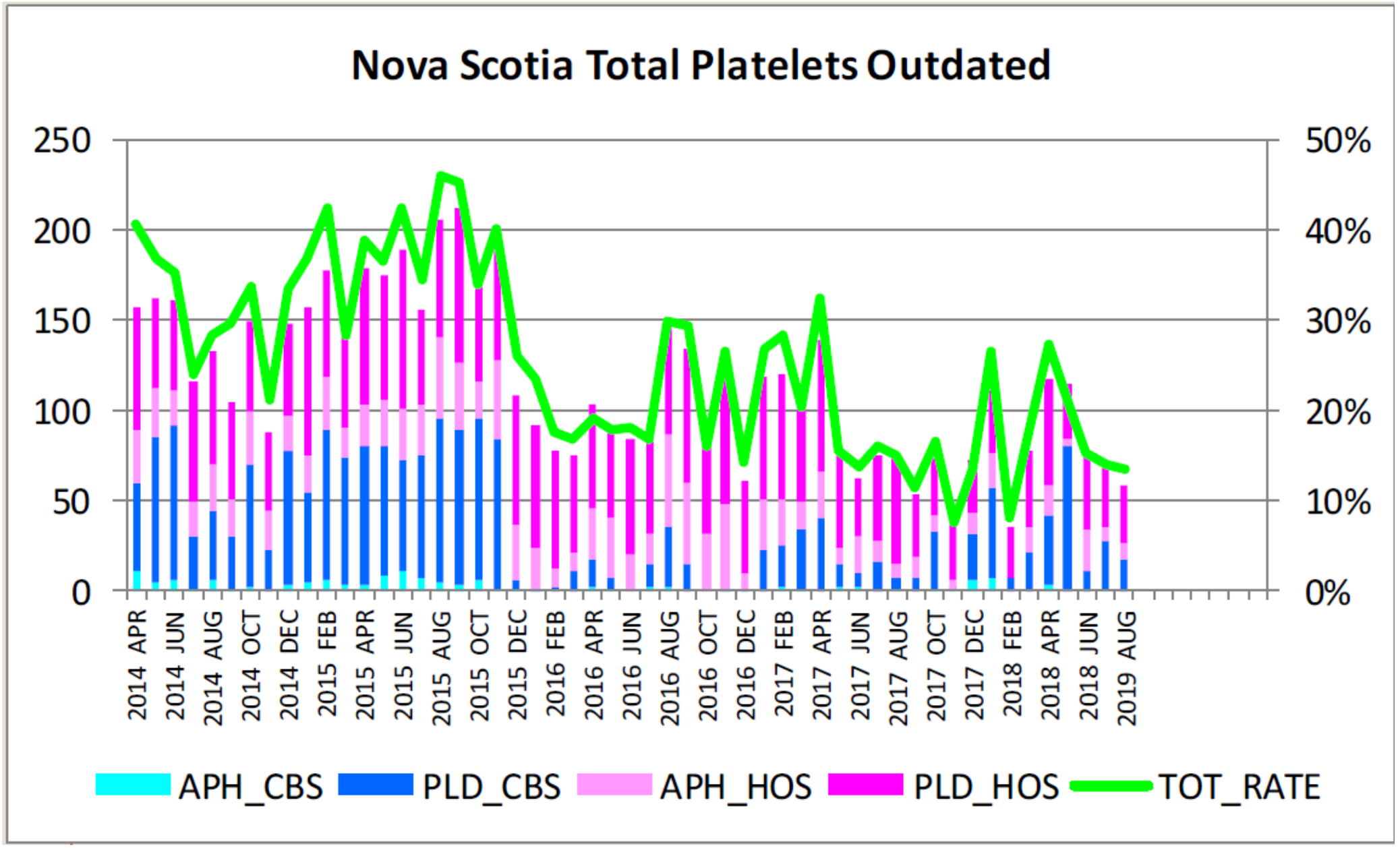

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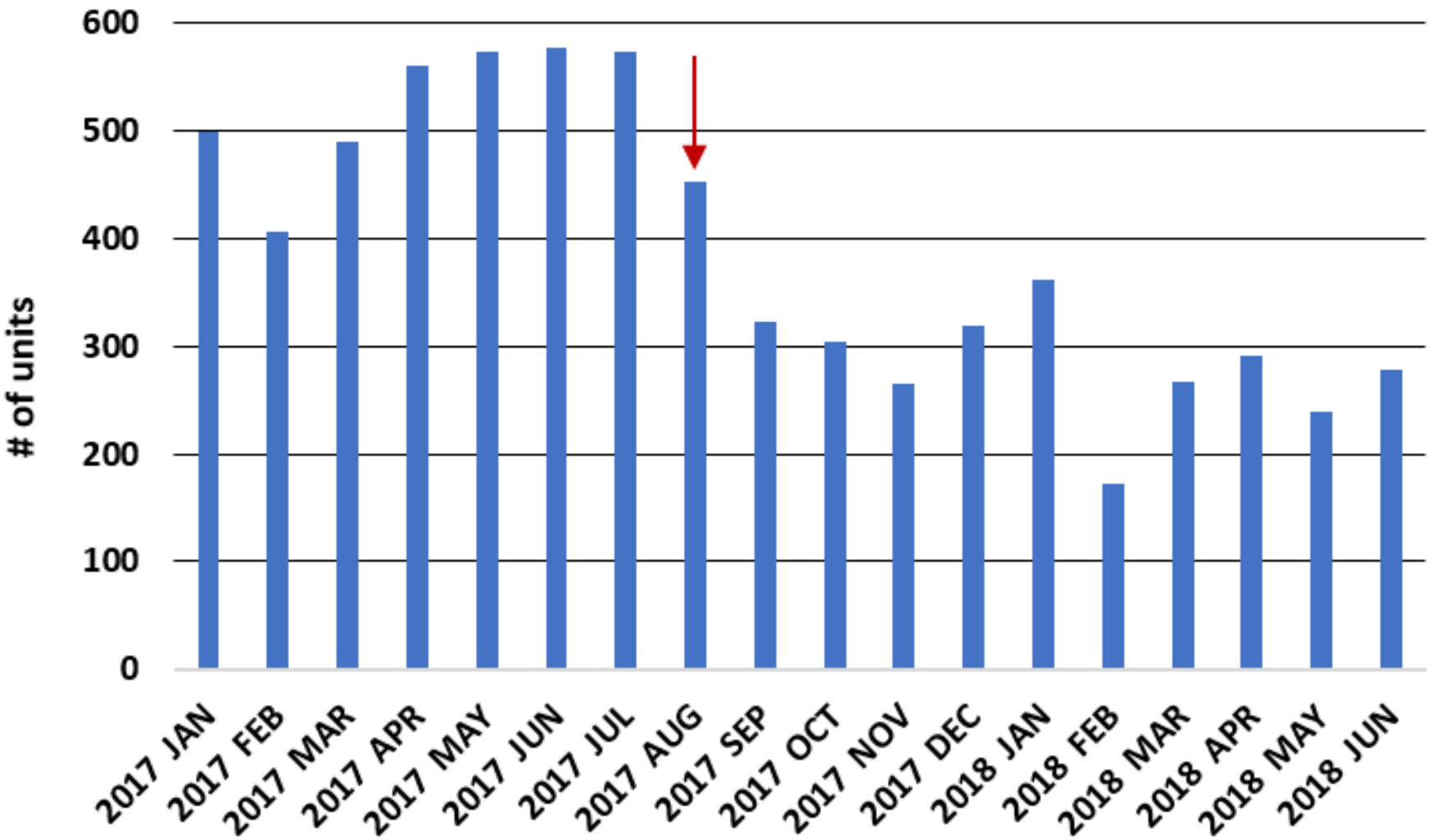
National Hospital Outdates, Apheresis platelets Jan 2017 to June 2018



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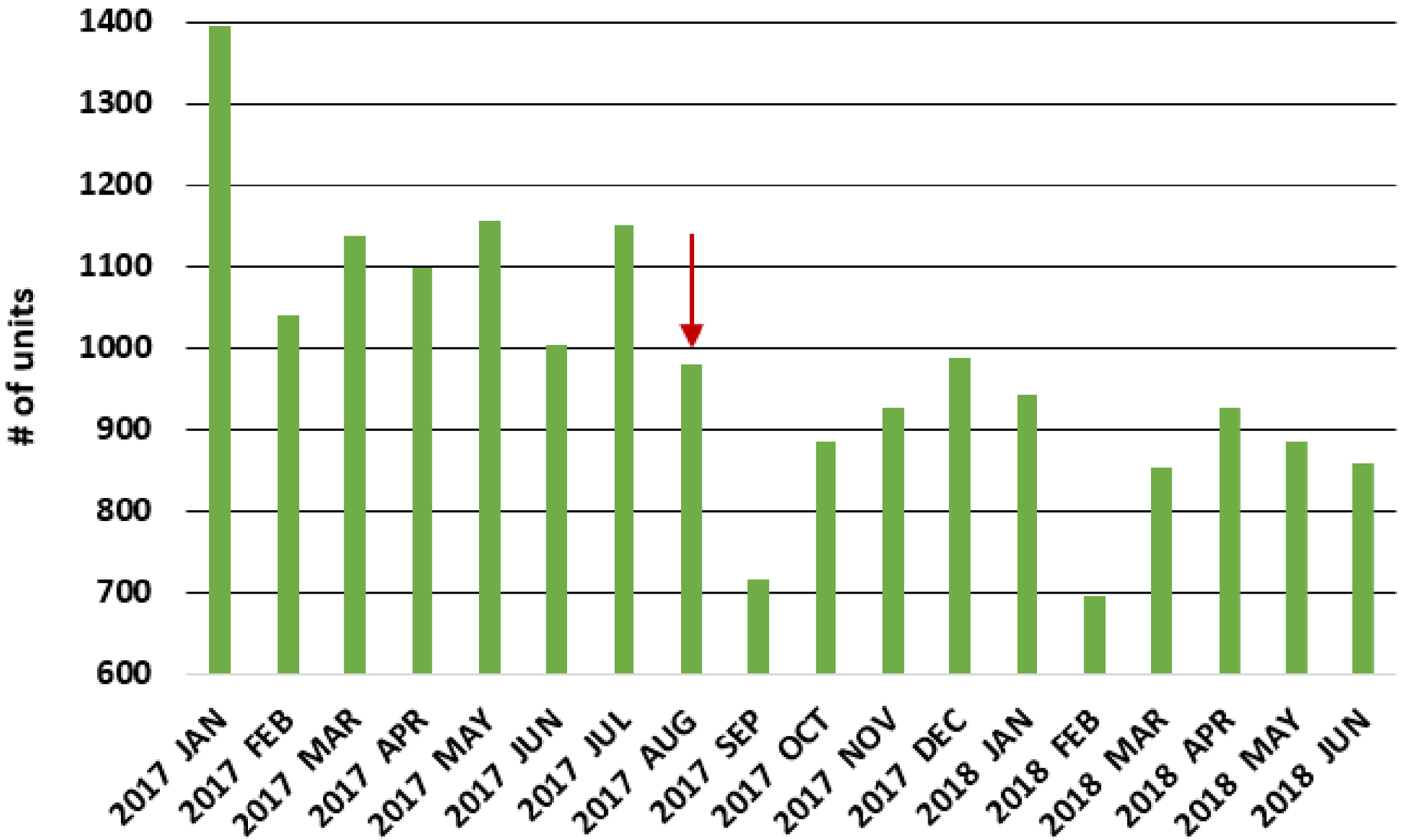
National Hospital Outdates, Buffy coat pools
Jan 2017 to June 2018



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Answers

1. The new protocol requires a longer pre-inoculation period and a post-inoculation hold, so a longer shelf life is needed. Increased sensitivity allowed a longer storage period.
2. More reports of possible bacterial contamination are due to increased number of culture bottles and addition of anaerobic bottle, with increased machine error and bacterial detection.
3. Very slow growing bacteria are still missed. In most cases, these are *P acnes*, and there has been no clinical symptoms associated with transfusion. More rarely, coagulase negative *Staph* are missed, and they may cause reactions.
4. A longer observation period is necessary to make firm conclusions about safety (rare missed significant bacteria). There has been a large decrease in platelet outdating.

Thank You

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Tammy Whitteker

Caesar DiFranco

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