“Difficult to Transfuse” Patients

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Case 1

- 10am – 45 yr old female with SCD, on monthly exchange transfusion programme – presented in A&E this am with small bowel obstruction.
  - Needs theatre for laparotomy – want 2 units of blood, as likely bleeding.
- **Patient O Ro with anti-C+E+Fy3+Jkb+S**
- 1 ‘wet’ unit in Colindale; 3 in Bristol.

What to do?

1. **Clinical urgency** –Surgeons want theatre in next 3 hrs – balance of risks.
2. **Blood Options –**
    1. Ag neg –
        1. 1 unit Colindale –“blue-light” 1-1.5 hrs door-to-door (hospital do XM, as no sample in RCI)

Case 1 ctd

2) 3 units in Bristol – even ‘blue-light’, too long;

3) 1 further unit in Colindale, but quarantined, as bled yesterday – awaiting virology results & WNV test.

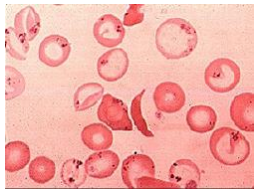
- Phoned – virology results in 2 hrs; get blood sent ‘blue-light’ to hospital (quarantine – HoL happy) & fax results as arrives.
- WNV – D/W Donor Drs – low risk (Italy); P Hewitt: not single + result on 23,478 tested that year, so risk low. Use & find result after.

2. Compromise on Ag neg blood –

  - ‘plan B’ blood: ABO, full Rh & K matched only, with IV methylpred 1g/kg & IVIg cover (1g/kg, or if renal function concerns, 0.4 g/kg – can repeat next day). Monitor for DHTR.
  - Not keen as already sick (bowel obstruction & for surgery); and risk of renal failure from DHTR – not ideal to add, if avoidable. But wd use, if units had not been available, or patient deteriorated & couldn’t wait.

Case 2

- Teenage female patient with SCD due for BMT in 2 weeks. Needs automated red cell exchange tomorrow, before BMT.



- Group O Ro with anti-C+E+S+Fy3+Jkb
- Want 10 units, <7 days old, HEV-
- Search: nationally total of 16 units ag neg blood; only 8 are <7 days old; only 2 HEV- (April 2016)

What to do?

1. **Clinical urgency** – not want to postpone, as donor lined up; & while patient well. Not want to exchange much closer to BMT, so within next 48 hr.

Case 2 ctd

2. **Blood options –**
    1. Ag neg units – lucky that have enough!
    2. <7 days old – 2 are 12 & 14 days old.
        - Rationale for BSH recommendation, is that red cells will last longer. But won't if incompatible with Ab! So override – ag neg takes priority.
    3. HEV neg (not an issue now, as universal testing).
        - Then, could not wait for prospectively tested units to come through; nor retrospective testing before proceed, as archives all over the country and central testing.
        - Override: give HEV untested blood, on balance of risks (risk then 1 in 1600 donors viraemic, <40% transmission by red cells ; can test after, and if PCR+ , can treat).
- BMT proceeded on time.

Challenges of Provision of Blood for Patients with SCD

In UK, **full Rh (CcDEe) & K matched** recommended for >20 years (BSH guidelines) as:

- ↓ Rh & K antibodies (constitute 80% Abs in broad patient population)
- Some evidence that ↓ development of **other** Abs beyond that

Where are we now re: extended matching?

- Desirable perhaps, but is it doable?
- ***Scale:** 99 patients (Colorado), over 13 years, average 70 units per patient (so av 6 units per year). (Matched for Fy, Jk, Ss).
- cf: Imperial alone has 47 patients in 6 months…. lot more than av 6 units per year!

- Not been able to implement in UK to date, as cannot meet demand

* *LaSalle-Williams, Transfusion (2011)*

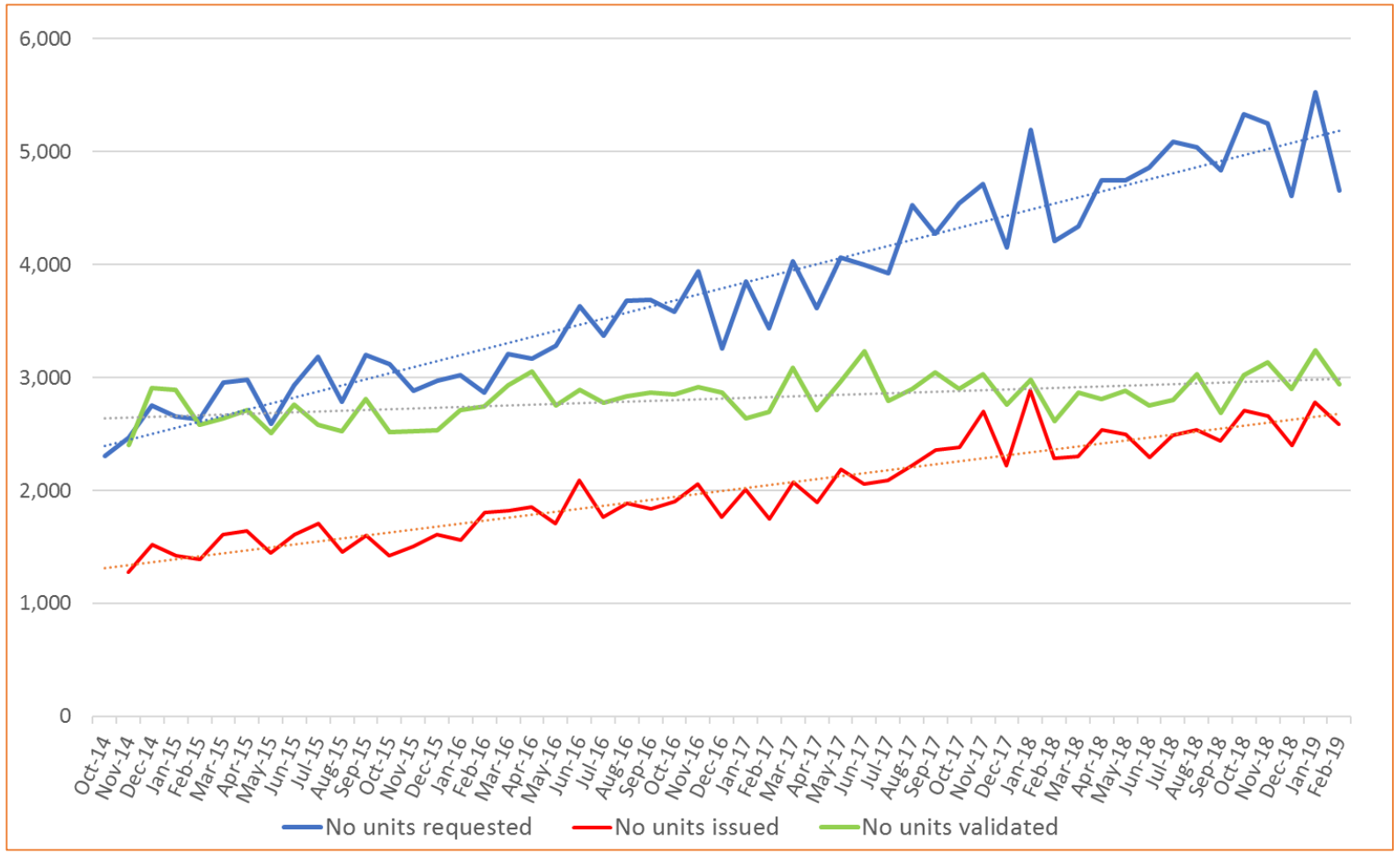
? Extended Matching ctd

At NHSBT, not enough units to do extended matching (MNSs, Fy, Jk) because:

- High throughput genotyping of donors not undertaken (yet) – cost++, different technologies evolving quickly: under review;

- Not all donor blood has extended phenotyping (by serology - labour intensive)
  - Despite several measures: ↑ testing, through policies (targeted testing most BAME donors); & only need to test 2x ever to label phenotype; KPIs for donor testing etc;
  - But resource-hungry – finite capacity of Donation Testing to do extended phenotyping, even on targeted population. Resources have ↑, but so has demand…..

Number of Ro units: Requested and Issued



Collection adherence	Feb 19
Ro collections, % of target	89.7%
Ro collections, % of demand	61.0%
% of units issued vs. validated	88.0%

- **Demand doubled since 2014**

Concern:

- **Cannot meet all demand now, for patients <u>WITH</u> antibodies,** who need multiple antigen negative blood – from total NHSBT blood supply;
    - if implement extended matching prophylactically for patients *without* corresponding antibodies ……
    - will jeopardise patients *with* antibodies, for whom corresponding antigen negative blood will not be available – with risk of DHTR (delayed haemolytic transfusion reaction) from incompatible blood.

Evidence for Unmet Demand for Clinical Need?

- March 2014 – May 2016: noted cases where not enough, or only just enough compatible blood, with no buffer for any further request for same or other patients:
- 40 cases:
    - multiple antibodies within the Rh, K Fy, Jk, MNSs systems (18).
    - Others – single antibodies e.g.: anti-U (10); Bombay (4); other (8).
- Stockbuilt for patients to have enough for one exchange at least (frozen) – occ just top-up

Case examples:

Type of blood	Clinical circumstances	Comments
c-E-k-Fya-Jka- 2 units	49 yr male with trauma – head injury, ventilated, Hb 60g/L – 2 units given; (none left)	If symptomatic or further ITU complications, risk to outcome.
O+ Ro K-E-S-Fy(a-b-) Jkb- **(as anti-E+S+Fy3+Jkb)** 6 units for exchange	SCD in ITU post-op (lap-cholecystectomy) with chest crisis. Hb32 g/L; O_2 sats falling. Blue light.	Just enough – no further in region (>7 days old). If gave blood not fully compatible (with IVIg cover) – could worsen already compromised renal function & chest crisis.
Anti-Fy3 +S+C+Jka 3-4 units	30 yr old male patient with SCD – Hb 37 g/L (not needed transfusion since 2010)	2 wet units only. Compromise on one Ab, with IVIg cover. Monitor & rescue DHTR. (Another SCD patient needing same phenotype, beforehand.)

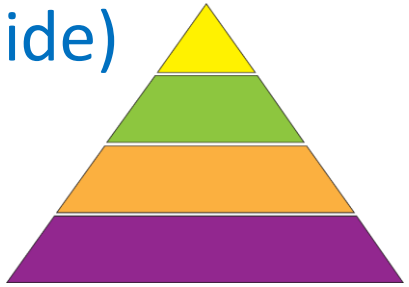
Forward:

- ↑ demand to continue:

- Ongoing plans to meet demand (March 2019):
  1. ↑ recruitment BAME donors – to find rare types (ongoing strategies >15 years);
     - 11,454 Black donors active in NHSBT;
     - 7172 donors donated 11,081 units last year. (Up from previous year: 5809 donors donated 9314 units).
  2. Optimise what already have on shelf - ↑extended ag typing (serology) of greater % of BAME donors (for multiple ag neg; U neg; Bombay etc);
  3. Genotyping – high throughput, cost-effective, best targeted donors;
     - Assuming universal donor genotyping is prohibitively expensive in short term; though technology advancing / reducing cost; (1.3 million blood donors in NHSBT).
     - Project to do extended genotyping (incl Rh variants) on an additional 4000 regularly donating Black donors;
     - Plan to inform optimum strategy for targeted genotyping – what proportion of the donor population; taking into account patient need / benefit; cost-effectiveness; and cost to hospitals.

4. Patient Prioritisation for Extended Matching:

1. Patients with multiple antibodies already;
2. Patients with SCD, with scan indications for regular exchange transfusion – but currently not enough blood available *(next slide)



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3. Prophylactic extended matching: ? All SCD / Thal / ±MDS / ± all transfusion dependent.
    - Maybe desirable, but balance of risks of depleting ag- blood for patients *with* Abs already. Definitely aim for.

Previously “Untransfusable” patients:

Last year, able to start 2 patients, with new indications for exchange programme (due to ↑phenotyping):

1. **Anti-C+M+S+Fya+Jkb+hrS antibodies** - needs group O **R2R2** M-S-Fya-Jkb- x8 units every 6 weeks (64 units pa); override <10 days old rule;

2. **Anti-S+Fyb+Jkb+Lua antibodies** – needs gp O Ro **S-Fyb-Jkb-** (Lua as x-match compatible). Also 6-8 units every 6-8 weeks (=36-64 units pa);

Survey nationally via Haemoglobinopathy Forum Spring 2020: (Sara Trompeter, Jo Howard & FR)

- to identify any other similar patients, who should be Tx’d, but thought can’t be:
  - to see if any possible measures to stock-build / capacity to call in enough donors to enable exchange programmes or top-up needs, as above. (114 patients suggested - working on)

Modelling for Future Demand Planning

- Looking at stock levels in a model, for different red cell phenotype requirements

  - **Requirements? Haemoglobinopathy Registry** to inform what blood needed nationally: (phenotypes), how much, how often. ST working to optimise data on Registry & link with NHSBT data on phenotypes required etc.

  - **Demand Planning:**
    - What stock would we need to meet current demand?
    - What would need if did extended matching – just in patients with an antibody?
    - What would need if extended matching in all patients with SCD?

- Project will take year+ as data gaps (Registry), complex modelling needed etc

Hyperhaemolysis – Tx Lab aspects

What Tx Lab needs to do:

1) Haemolysis? - Hb, LDH, bilirubin, retics, film

2) urine: haemoglobinuria? - If so & if hyperhaemolysis suspected - %HbS & HbA (on plasma, if no Hb'uria).

3) **Pre- & post-Tx: G&S** - ? **new** allo-antibody causing DHTR;

4) **DAT** – if pos, do **eluate** (? low level new Ab, on transfused red cells, but none spare for detection in plasma)

5) If "auto-Ab" to an Rh ag – ? has patient got **Rh variant** ag (eg: e or C or D etc) – genotype at IBGRL

6) **Selection of blood:** if needed.

- **Select ABO, full Rh & K matched** – and negative for any ag(s) to which any Abs. X-match.
- If id of new alloantibody is uncertain despite further Ref Lab testing, consider extended matched blood (Fy, Jk, Ss) - if extended phenotype / genotype known & blood available & time permits.
    - Consider IVIg +/or steroid cover.