Polycythaemia

Introduction
The major determinant of blood viscosity is the haematocrit. Polycythaemia is generally defined as a central haematocrit of 65% or more. The viscosity of blood rises exponentially above a haematocrit of 65%. However, not all infants who are polycythaemic have hyperviscosity. Blood viscosity correlates better with symptoms than the haematocrit, highlighting that haematocrit is not the only determinant of blood viscosity. As blood viscosity is not easily measured in the nursery, haematocrit is usually used as the basis for diagnosis and treatment. Studies of partial exchange transfusion have yet to show unequivocal benefits.

Incidence and risk factors
Polycythaemia (venous haematocrit >65%) occurred in approximately 4% of newborn infants. Symptomatic polycythaemia occurs in 0.4-0.6% of screened infants. Hyperviscosity (>2sd above population mean) occurred in 5% of infants. Hyperviscosity was invariable with a venous haematocrit > 65%, but also occurred in some infants with a haematocrit 60-64%. Risk factors for polycythaemia include:

1. Increased erythropoiesis due to:
   - Intrauterine hypoxia (placental insufficiency associated with growth restriction, hypertension or maternal smoking)
   - Endocrine disorders including maternal diabetes, neonatal thyrotoxicosis and congenital adrenal hyperplasia, and
   - Chromosomal abnormalities including Down syndrome (trisomy 21).

2. Erythrocyte transfusion due to:
   - Twin to twin transfusion (monochorionic twins)
   - Maternal-fetal transfusion (theoretical)

Delayed cord clamping has been suggested, but meta-analysis of trials at term show a non significant increase in polycythaemia. A recent RCT of term babies in Sweden has also not shown an increase in polycythaemia.
Cord milking has also been shown, in a recent RCT, not to increase the risk of polycythaemia.32

Consequences
Polycythaemia refers to an increased red cell mass. The clinical features associated with polycythaemia have been attributed to hyperviscosity4,11 associated with a high haematocrit, but also to hypervolaemia4 in some infants. The viscosity rises exponentially above haematocrits > 65%. Hyperviscosity results in abnormal blood flow kinetics (increased 'stickiness' of blood) and may result in tissue hypoperfusion. Clearly, many of these features are difficult to differentiate from infants with other diseases of the newborn period (eg neonatal encephalopathy, respiratory distress syndrome). Many of these features may be associations rather than consequences of hyperviscosity. The clinical features ascribed to polycythaemia include:

- **Central nervous system:** Early changes include hypotonia, poor arousal, poor suck, vomiting, irritability and jitteriness (these signs may be due to underlying condition such as hypoglycaemia in infant of a diabetic mother).

- **Metabolic:** hypoglycaemia is common in polycythaemic infants11.

- **Cardiac and pulmonary:** tachypnoea, tachycardia and cyanosis occur in up to 50% of hyperviscous neonates. Chest x-ray may demonstrate cardiomegaly and elevated pulmonary vascular resistance has been demonstrated on echocardiography.11

- **Renal:** findings are variable depending on whether there is associated hypervolaemia.

- **Gastrointestinal:** Poor feeding is frequent, and necrotising enterocolitis may be associated12,13, although there are concerns that NEC may be more frequent in those infants receiving partial plasma exchange for hyperviscosity16.

- **Haematological:** Mild thrombocytopenia is common, but thrombosis is rare.

- **Neurodevelopment:** infants with hyperviscosity are at increased risk of motor and neurological abnormalities14,15. Hyperviscosity correlates better with adverse outcomes that polycythemia14,15.
Diagnosis

A haematocrit is not routine for babies admitted to the nursery. The most common clinical indications for performing a venous haematocrit (full blood count) are extreme intrauterine growth restriction (birth weight < 3rd percentile) and monochorionic twin pregnancy where twin-twin transfusion is suspected. As blood viscosity measurements are not easily available, perform haematocrit on cord blood (if suspected early) or on a central venous sample (venupuncture). Either microcentrifuge 3000rpm for 4 minutes (available in the NICU) or use the laboratory analyser measurement (which is usually slightly lower due to trapped plasma).

Polycythaemia is generally defined as a central haematocrit >65%\textsuperscript{4, 11}. Factors that need to be taken into account when interpreting haematocrit results\textsuperscript{11}:

1. Age of infant at sampling - haematocrit peaks at 2 hours of age, then falls over next 6-24 hours.
2. Site of sampling - capillary sample significantly higher than central (venous or arterial) sample.
3. Method of analysis - microcentrifuge haematocrit slightly higher than haematology analyser.

Treatment

Partial volume exchange transfusion:

PVET corrects the polycythaemia and hyperviscosity, however Improvements in clinical signs have not been unequivocally documented in randomised trials of PVET compared to no exchange\textsuperscript{16-19}. Improvements in infant symptoms as measured by the Brazelton Neonatal Behavioural Assessment Scales\textsuperscript{17} were reported by one study. However, rates of feeding difficulties were increased after plasma exchange in one trial\textsuperscript{16}. One study has shown short term improved cerebral oxygenation in infants with haematocrit > 70% or 65% with symptoms\textsuperscript{36}

No evidence of benefit in mortality or long term developmental outcome\textsuperscript{16, 17, 33, 34, 35} has been shown from partial volume exchange transfusion (PVET) in infants with symptomatic or asymptomatic polycythaemia.

There are also potential harms. Necrotising enterocolitis is increased following treatment for asymptomatic polycythaemia\textsuperscript{34, 35}. 
A lack of proven benefit of PVET in infants with polycythaemia / hyperviscosity may have several explanations. Firstly, all trials randomised infants with predominantly asymptomatic polycythaemia\textsuperscript{16-19} and so the trials may be insufficiently powered to detect a benefit. Secondly, although PVET improves cardiac function\textsuperscript{25-27} and cerebral blood flow\textsuperscript{28, 29}, there is no associated improvement in cerebral oxygen delivery\textsuperscript{27, 28}. This has recently been challenged \textsuperscript{36}.

**Plasma versus normal saline:**

Several studies have compared a form of colloid (fresh frozen plasma or albumin) with crystalloid (normal saline or Ringer's solution) and found no short-term differences in outcomes\textsuperscript{20-24}. Normal saline is the preferred option\textsuperscript{37, 38}.

**Our policy:**

*There is no evidence that exchanging asymptomatic infants is of any benefit. As there is insufficient evidence to guide practice, PVET will usually be used where there are unequivocal symptoms associated with severe polycythaemia. Consider treatment if either:*

1. Infant symptomatic and haematocrit > 70%

*Or*

2. Haematocrit > 75%.

**Volume of normal saline exchanged is:**

\[
\text{Volume Normal saline (ml)} = \frac{\text{Total blood volume} \times (\text{Observed PCV} - \text{Desired PCV}[0.55])}{\text{Observed PCV}}
\]

**Example:**

For a 1Kg baby: Haematocrit = 0.75

\[
\begin{align*}
\text{Blood volume} & = 80\text{ml/kg} \times 1\text{kg} = 80\text{mls} \\
\text{Volume saline} & = 80 \times (0.75 - 0.55) / 0.75 \\
& = 80 \times 0.2 / 0.75 \\
& = 16 / 0.75 \\
& = 21 \text{mls}
\end{align*}
\]

Alternatively, just using 20ml/kg normal saline is usually satisfactory.
How to perform a partial exchange transfusion

Use a combination of either umbilical or peripheral arterial and venous lines. The exchange should use the iso-volumic technique ie. withdraw blood at the same rate as infusing normal saline. The procedure should take at least 30 minutes.

Key Points:

<table>
<thead>
<tr>
<th>Statement</th>
<th>Level of Evidence</th>
<th>Strength of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>The major determinant of blood viscosity is the haematocrit.</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Polycythaemia is defined as a central haematocrit ≥ 65%</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>The viscosity of blood rises exponentially above a haematocrit of 65%</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Not all infants who have hyperviscosity are polycythaemic</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Symptoms and outcome relate better with blood viscosity than haematocrit</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Studies of partial exchange transfusion have yet to show unequivocal</td>
<td>1a</td>
<td>A</td>
</tr>
<tr>
<td>benefits.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal saline is as efficacious for partial volume exchange as colloid.</td>
<td>1a</td>
<td>A</td>
</tr>
<tr>
<td>Partial exchange transfusion carries a risk of necrotising enterocolitis</td>
<td>1a</td>
<td></td>
</tr>
</tbody>
</table>
References


36. Ergenekon E, Hirfanoglu IM, Turan O, Beken S, Gucuyener K, Atalay Y. Partial exchange transfusion results in increased cerebral oxygenation


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Revised Dr Girvan Malcolm  November 2013
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