

**TRALI – Clinical  
Mimicry, making the  
diagnosis**

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# TRALI

- First recognised as a distinct clinical entity in 1985
  - case reports from as early as 1951
- Important, potentially life threatening
  - Currently a leading cause of transfusion related death
- Increased risk associated with some conditions
  - cardiac surgery
  - haematological malignancy during induction chemotherapy
- increasing incidence
  - ?? increasing blood use / aggressive transfusion
  - ?? better recognition

# TRALI Definition (NIH)

- **TRALI without clinical risk factors for ALI**
  - New ALI temporally related to transfusion\*
  - Worsening of pre existing pulmonary insufficiency temporally related to transfusion
- **TRALI with clinical risk factors for ALI**
  - New ALI temporally related to transfusion\*
  - New ALI thought to be mechanistically related to transfusion
  - Worsening of pre existing pulmonary insufficiency temporally related to transfusion

\*New onset (<6hours from transfusion); hypoxemia  $SpO_2 < 90\%$  or  $PaO_2/FiO_2 < 300$  mm Hg on room air, or other clinical evidence of hypoxemia, bilateral infiltrates on frontal chest X-ray

# Canadian Consensus Conference

## Panel TRALI

- TRALI Acute lung injury (ALI\*)  
Occurring within 6 hours of completion of transfusion of blood component.  
No pre-existing\*\* acute lung injury.  
No other temporally associated risk factors# for acute lung injury
- Possible TRALI Acute lung injury  
Occurring within 6 hours of completion of transfusion of blood components  
No pre-existing\*\* acute lung injury.  
One or more temporally associated risk factors# for acute lung injury

\*\*Pre existing conditions - Aspiration Pneumonia, Toxic inhalation, Lung contusion, Near Drowning

# Risk Factors - Severe sepsis, Shock, Multiple trauma, Burn injury, Acute pancreatitis, Cardiopulmonary bypass

**Final results depend on direction you choose**



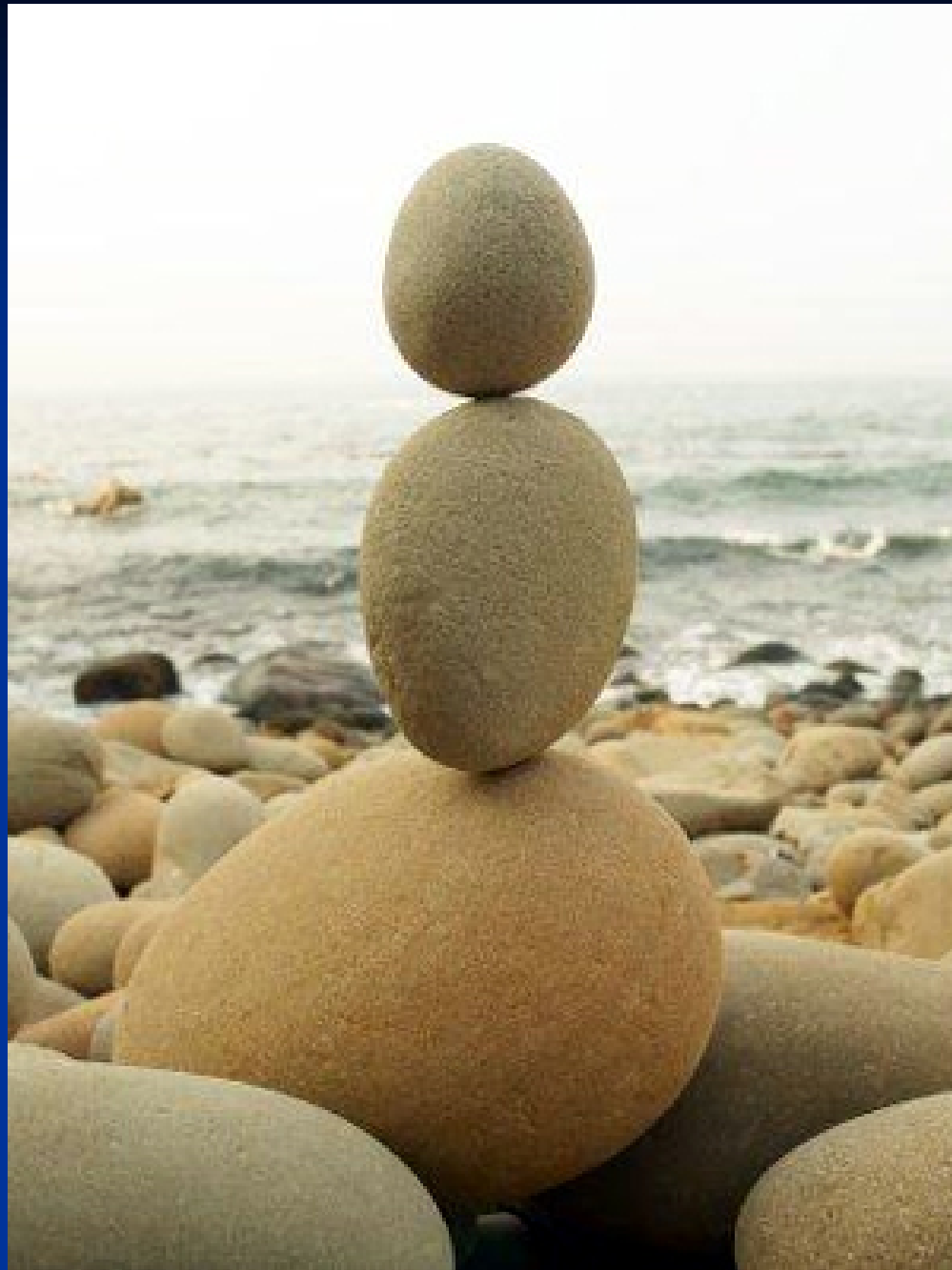
# TRALI – problems of identification

- Incidence is unclear (1:1300 USA – 1: 100,000 Canada)
  - dependent on definition applied
  - exclusion criteria significantly affect this
- Variable clinical spectrum
  - Classic case (ARDS like) -non cardiogenic pulmonary oedema
  - Milder reactions
    - incomplete clinical symptoms
    - less likely to recognise
    - may recover without intervention
    - some may mimic FNHTR's
- Whether it is considered in complex clinical situations
  - Differentiation from infection / ARDS / Other transfusion related complications

# What transfusions are potentially a problem?

## When do I need to think about it?

- Any plasma containing products (esp if  $> 60\text{ml}$  plasma involved)
  - FFP
  - Platelet concentrates
  - Whole blood
  - RCC
  - Granulocytes
  - IVIg / cryoprecipitate (rare but described)



# Case 1

- 2year old Downs Syndrome child
- AML evolved from MDS
- Chemotherapy, multiply transfused
- Thrombocytopenia requiring treatment during last course of therapy
- Intercurrent mild URTI – sniffly nose only
- Transfused 2 units platelet concentrate

# Case 1

- Acute reaction
  - onset of respiratory distress during infusion
  - Desaturated on oximetry
  - Tachycardic, peripheral shut down
  - CXR - fluffy infiltrates
- MANAGEMENT
  - Transfusion ceased
  - Oxygen via mask
  - Lasix
  - Observe in ICU
- Improved over 12 - 24 hours to pre transfusion state

# Case 1

## ■ Possible Diagnoses

- Fluid overload
  - possible but no gross change in fluid load ( platelets ~200mls)
- Allergic/anaphylactoid
  - not classic in terms of severity or other manifestations
- Infective
  - recipient had URTI ? possible evolution, but sudden deterioration and early recovery
- TRALI
  - could fit within spectrum, ? Role of URTI in increased risk

# Case 1

## ■ Investigation

### ■ Cultures

- platelet concentrate negative
- recipient negative

### ■ IgA total and subclasses normal

### ■ Antigranulocyte Abs

- present in donor sample of one platelet unit
- compatibility testing vs recipient
- reactivity (confirmed x 2 separate occasions)

FINAL DIAGNOSIS - TRALI



# Case 2

- 14 yr female with Acute Promyelocytic Leukaemia
  - Bleeding gums, bruising ++.
  - Hepatosplenomegaly
  - Chest clear, no respiratory symptoms
  - WCC  $59 \times 10^9/L$ , blasts and abnormal promyelocytes
  - Platelets 10,000
  - Hypofibrinogenemia (1.1g/L), PT 15secs (NR 9 -14s), DDIMER 15.62 ( $<0.28\text{mg/L}$ )
  - Platelets and FFP prescribed

# Case 2

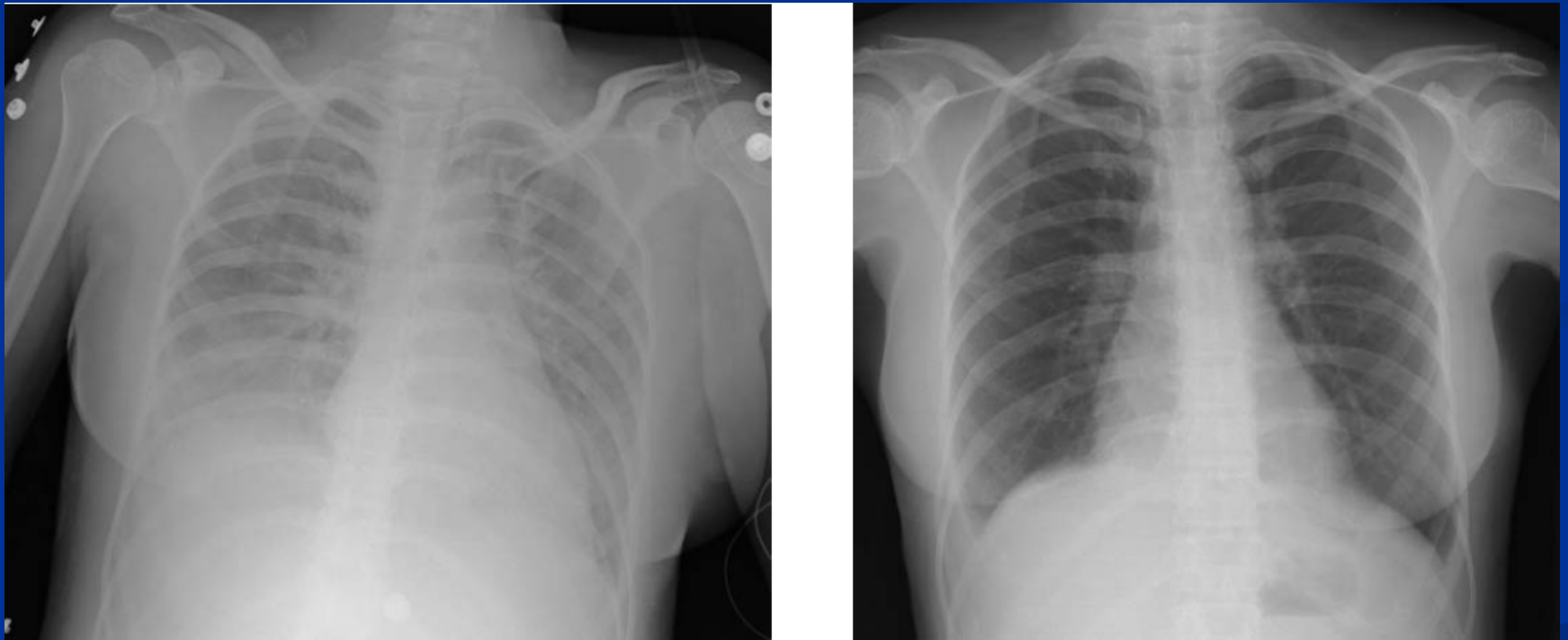
- 3 Infusions of FFP over 36 hours
  - #1 – urticaria on abdomen
    - Settled with hydrocortisone / phenergan
  - #2 – 6 hours later
    - premed of hydrocortisone / phenergan
    - Fever, rigors, hypotension
    - increased respiratory rate, mild desaturation with oxygen requirement which settled over a few hours
    - FFP ceased
    - Fluid bolus, cultures taken and broad spectrum antibiotics commenced
    - ?? Infective

# Case 2

- #3 commenced 12 hours later
  - Again febrile with rigors, hypotension and vomiting
  - Severe desaturation with progressive deterioration and increasing oxygen requirement over next few hours
  - Coarse crackles and reduced air entry
  - Complaining of chest pain
  - CXR – hilar streaking, fluffy opacities and fluid in fissures
    - ? Infection ? Overload ? Pneumonitis related to APML
    - ?? TRALI

# Case 2

## Presentation and Recovery



# Case 2

## ■ Transfer to PICU

- NO further FFP ( coagulopathy managed with rVIIa and platelets)
- Given steroids ( to reduce effects of hyperleucocytosis)
- Given Lasix
- AML Chemotherapy commenced

## ■ Progress

- High O2 requirement via mask
- Not ventilated
- Oxygen ceased 16 days later
- No recurrence

# Case 2

- Normal IgA
- Cultures negative
- TRALI Investigation
  - **Patient** - White cell antibodies not detected in pre-transfusion sample.
  - **Donor results**
  - No WBC antibodies in donor 4128807, but cross match incompatibility between donor plasma and patient neutrophils supports the clinical diagnosis of TRALI.
  - It is more difficult to determine the significance of the neutrophil and HLA (class I and class II) antibodies in donor of 4617515 as cross match results are lacking. The presence of these antibodies, however, also supports a clinical diagnosis of TRALI.
  - Other donor testing not contributory

# Case 2

- Presumed final diagnosis
  - TRALI
  - Difficult to exclude some additive and or local effect on lungs of abnormal promyelocytes and blasts
- BUT
  - Temporal relationship of acute deterioration to FFP infusion strongly supports a transfusion induced event
  - Clinical course also supports this assumption



# Diagnosis

- Diagnosis of exclusion
  - consider it a possibility
    - clinical scenario + onset of symptoms within 6hr of transfusion of plasma containing product
  - exclude other causes for respiratory distress
    - transfusion related or otherwise
  - initiate specific testing ( even if not sure it is TRALI)
    - liaison with appropriate laboratory service
    - access samples from patient and donors
    - screen for anti granulocyte, anti HLA antibodies in donor and recipient
    - confirm with donor recipient leucocyte cross match
    - follow up testing as required

# Differential Diagnosis

## Transfusion related reactions

### ■ TACO

- Related to large volumes, or poor ability to accommodate lesser volumes (eg renal / cardiac impairment)
- Responds quickly to aggressive diuresis and ventilatory support

### ■ Anaphylaxis

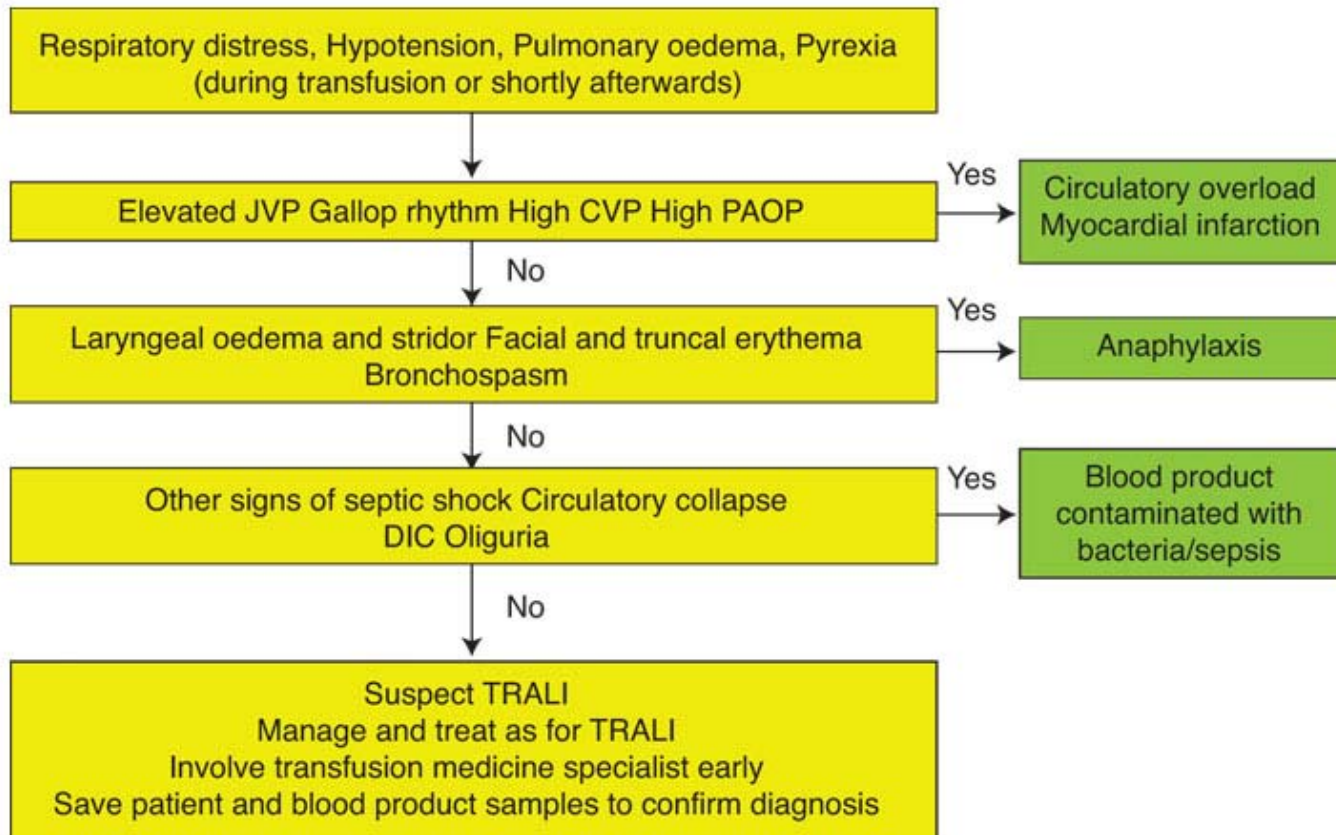
- Laryngeal oedema and bronchospasm, with wheeze / stridor
- Usually facial / tongue swelling
- Urticaria of face, upper trunk frequent
- Often after only small volumes of any blood product

### ■ Infection

- Platelets or red cells, need to consider if any pulmonary insufficiency

### ■ Immediate Haemolytic Reaction

- Usually readily distinguished by presence of haemolysis



# ARDS vs TRALI

## ARDS

- Insidious
- **Clinical presentation**
  - Hypoxic respiratory failure
  - High PaO<sub>2</sub>/ FiO<sub>2</sub> ratio
  - Reduced lung compliance
  - Diffuse infiltrates on CXR
- **Management**
  - Maintain adequate oxygenation, prevent iatrogenic lung injury
- **Prognosis**
  - Prolonged ventilation associated with multi-organ failure.
  - Resolution with fibrosis may cause permanent impairment of gas exchange
- **Mortality**
  - 30-60%

## TRALI

- Acute
- **Clinical presentation**
  - Always within 1-6 hours of transfusion
  - If severe may mimic ARDS
- **Management**
  - As for ARDS
- **Prognosis**
  - Improvement occurs in 48-96 hours with correction of PaO<sub>2</sub>/ FiO<sub>2</sub> ratio in most cases
  - Some take >7 – 10days to recover
- **Mortality**
  - 5% (some studies suggest up to 25%)



# Why is it an important diagnosis??

- Recognition influences care of the patient
- Mainstays of therapy = Supportive care
  - Ranges from supplemental oxygen to ventilation
  - Circulatory management as required
  - No role for diuretics or steroids
    - BUT
    - not always clear what you are dealing with
    - treatments are often “empiric”
    - especially in very sick patients

# Important implications for others

- Potential adverse effects on other recipients of products from these donors
- Withdrawal / disposal of implicated products
- Donor deferral
- Research

# Transfusion related acute lung injury - TRALI

- Important form of transfusion reaction
- Should be identified or at least considered in any relevant clinical situation – ALI within 6 hours of transfusion
- Prompt recognition / suspicion allows for appropriate investigation and treatment
- Allows anticipation of likely outcome – particularly relevant for the patient / counselling
- AND
- Detection of donors whose plasma poses a risk - deferral / research

