# Transfusion-Associated Dyspnoea (TAD) n=21

# 17c

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## Definition:

**TAD is characterised by respiratory distress within 24 hours of transfusion that does not meet the criteria for transfusion-related acute lung injury (TRALI) or transfusion-associated circulatory overload (TACO) or allergic reaction. Respiratory distress in such cases should not be adequately explained by the patient's underlying condition (International Society of Blood Transfusion (ISBT) definition).**

## Key SHOT messages

- Pathophysiology of transfusion-associated dyspnoea (TAD) is still not known and with no definite diagnostic criteria, our understanding is evolving
- Cases submitted are reviewed by SHOT experts including pulmonologists to determine imputability, causality and categorisation
- Further international collaboration in this area will help identify causal and contributory factors and identify appropriate risk reduction measures

## Abbreviations used in this chapter

| | | | |
|---|---|---|---|
| **AML** | Acute myeloid leukaemia | **ISBT** | International Society of Blood Transfusion |
| **ARDS** | Acute respiratory distress syndrome | **NIDDM** | Non-insulin dependent diabetes mellitus |
| **COPD** | Chronic obstructive pulmonary disease | **TACO** | Transfusion-associated circulatory overload |
| **CPAP** | Continuous positive airway pressure | **TAD** | Transfusion associated dyspnoea |
| **CXR** | Chest X-ray | **TRALI** | Transfusion-related acute lung injury |
| **FAHR** | Febrile, allergic and hypotensive reactions | **WCC** | White cell count |
| **IHN** | International Haemovigilance Network | **WEG** | Working Expert Group |

## Recommendation

- Patients who develop respiratory distress during or up to 24 hours following transfusion where transfusion is suspected to be the cause must be reported to SHOT

**Action: All staff involved in transfusion**

## Introduction

TAD is a pulmonary complication post transfusion that cannot be classified as TACO or TRALI, nor can it be ascribed to patient's pre-existing diseases. The underlying risk factors and aetiopathogenesis

are still unknown. Although such reactions are not very common, knowledge about them can prevent serious complications. Early recognition and prompt supportive treatment is beneficial. Appropriate risk reduction strategies are only possible once we understand these reactions better.

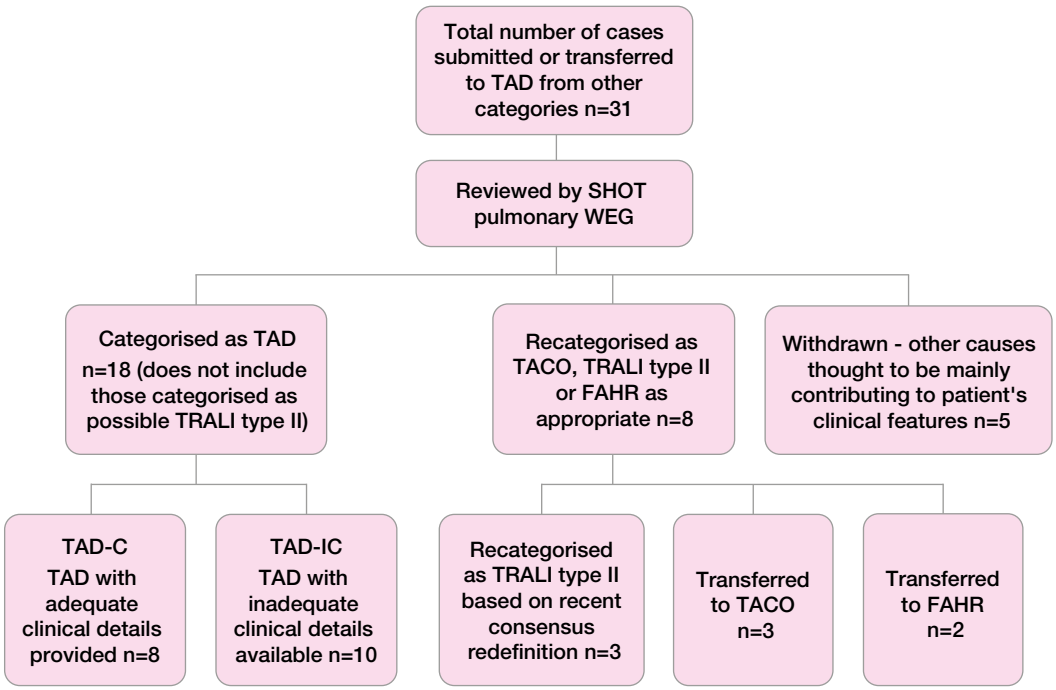
There has been significant international collaborative work relating to pulmonary complications post transfusion, most notably with TACO and TRALI. A new surveillance definition for TACO, published in 2019 (Wiersum-Osselton et al. 2019), was the culmination of several years of collaborative work between the International Haemovigilance Network (IHN), AABB, and the ISBT. The new proposed revised consensus criteria for TRALI (Vlaar et al. 2019), the term 'possible TRALI' has been dropped. The terminology of TRALI type I (without an acute respiratory distress syndrome (ARDS) risk factor) and TRALI type II (with an ARDS risk factor or with mild existing ARDS) has been proposed. It suggests that cases with an ARDS risk factor that meet ARDS diagnostic criteria and where respiratory deterioration over the 12 hours before transfusion implicates the risk factor as causative should be classified as ARDS. According to this, TRALI remains a clinical diagnosis and does not require detection of cognate white blood cell antibodies. While this may help in clinical differentiation, this needs validating with real-life case scenarios to understand the implications to haemovigilance especially from the perspective of appropriate risk reduction preventative measures.

SHOT has recruited two experts from pulmonary medicine as part of the pulmonary WEG and all reported cases from 2019 were reviewed by the group. Interpretation was limited in several cases by the available clinical information including results from relevant investigations. The group applied the new proposed TRALI consensus definitions to those cases reported under TAD to see if it helped re-categorise these reactions. There were 3 cases categorised as TRALI type II which were non-immune TRALI. They are detailed below.

Those that are included under TAD were subdivided based on adequacy of the clinical information available, TAD-C (those with complete or adequate clinical information) and TAD-IC, those with inadequate information. As is usual, there were a few transfers between categories (febrile, allergic and hypotensive reactions (FAHR), TACO, TRALI, etc.) reflective of the challenges involved in interpreting these complex cases. All cases are included in order to build up the series of cases over time. A deep dive into all cases of TAD reported to SHOT over the years is being planned soon to identify common themes. TAD represents cases with atypical or overlapping entities with varying severity of reaction and impact on patients, and with currently unexplained pathophysiology.

The following figure summarises the categorisation and transfer of these cases.

**Figure 17c.1: Summary of transfers and categorisation of cases included under TAD**



## Death n=1

**Case 17c.1: TAD-IC**

*A man with known chronic obstructive pulmonary disease (COPD) in his 80s admitted with suspected sepsis with leucocytosis (white cell count (WCC) >30x10$^9$/L) developed acute dyspnoea with no wheeze/rash and deteriorated suddenly during red cell transfusion with tachypnoea and tachycardia, hypoxia ($O_2$ saturations 78%) temperature 37.7°C with bilateral transmitted sounds. He was not reported to have any concomitant cardiac or renal disease. Due to sudden deterioration, investigations could not be completed to ascertain cause.*

In view of sudden onset dyspnoea, paucity of clinical information and temporal correlation with transfusion, this has been included in the TAD-IC category.

## Major morbidity n=4

In 2019 there were 4 cases included as major morbidity. These include 1 case categorised as TAD-C (Case 17c.2), and the 3 cases of TRALI type II described below were admitted to intensive care as a result of the transfusion.

**Case 17c.2: TAD-C**

*A patient in her 80s was admitted with symptomatic anaemia and a 3-week history of worsening breathlessness and leg oedema. Other co-morbidities included acute on chronic renal failure (stage 3), non-insulin dependent diabetes mellitus (NIDDM), hypertension, cardiac failure with oedema. She was reported to have become more breathless 3 hours after the start of a unit of packed red cells with tachypnoea and desaturation: her oxygen saturation (on 10L $O_2$) dropped from 91% to 87%. Chest X-ray (CXR) showed an area of developing consolidation.*

While there were clinical risk factors for TACO, she was in a negative fluid balance, on regular diuretics with minimal or no response to repeat diuretics and bronchodilators. Chest infection could be contributory and has been included here to highlight the need to monitor such complex patients during transfusions due to the potential for sudden deterioration in clinical status necessitating prompt supportive measures and appropriate treatment. The patient needed continuous positive airway pressure (CPAP) and oxygen support and recovered from this episode.

## TRALI type II as per redefinition consensus criteria n=3

**Case 17c.3: Imputability-2 (Probable)**

*A young patient in his 30s diagnosed with acute myeloid leukaemia (AML) on induction chemotherapy developed rigors within 2 hours of platelet transfusion, with a rise in temperature of 2.4°C, tachycardia, desaturation, and wheeze. The CXR showed ARDS with progression from the previous one.*

This case was initially reported under TRALI and investigated for antibodies but not all donors responded when contacted. The patient had haemoptysis on the morning of the incident and eventually died due to non-transfusion related causes.

**Case 17c.4: Imputability-1 (Possible)**

*A woman in her 70s with pre-existing COPD and asthma became hypoxic, tachypnoeic and tachycardic within 1.5 hours of platelet transfusion. Cultures were negative, serology was negative and CXR showed bilateral ground glass appearance. The patient recovered following treatment with steroids, antihistamines and supportive measures.*

**Case 17c.5: Imputability-1 (Possible)**

*A patient in her 40s following surgery for breast carcinoma required massive transfusion, needing several blood components desaturated to 68% with hypotension, no evidence of fluid overload and bilateral patchy infiltrates on CXR. There was no evidence of cardiac, renal or respiratory disease and the donor antibody screen was negative. The patient needed CPAP support and recovered.*

## Learning point

- Clinicians should report all cases of post-transfusion pulmonary complications to the transfusion service so that further investigation can allow for further classification of such cases. There are cases where such distinction may not always be possible

## Conclusion

Most patients classified as TAD are very unwell with multiple ongoing issues. Some of these had features suggestive of TACO or TRALI but not enough reported detail to meet the SHOT criteria and hence included here. The pathophysiology of this group of complications requires further elucidation (Badami et al. 2015). There is some evidence that patients with sepsis are more at risk of respiratory complications following transfusion (Roubinian 2018), a reminder that every transfusion, particularly of platelets, a rich source of biological response modifiers, (Garraud et al. 2013; Garraud et al. 2016), should be reviewed to ensure it is indicated. There is still much work that needs to be done to understand cases reported under TAD, this is limited by the clinical information available and co-morbidities.

## References

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