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Easily Missed? Acute Aortic Syndrome

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What you need to know

- Consider the possibility of acute aortic syndrome in all patients presenting with chest pain that is unexplained or associated with a high-risk condition, pain feature, or examination finding in the Aortic Dissection Detection Risk Score.
- Undertake immediate CT angiography if the patient is acutely unwell and has characteristic features of acute aortic syndrome.
- Consider using D-dimer as an alternative to CT angiography for ruling out acute aortic syndrome in patients who have a high-risk feature, but the diagnosis is considered unlikely.

Easily Missed? Acute Aortic Syndrome

Case

A healthy mid-50s woman experienced sudden, tearing pain, like a lightning bolt from her neck to her chest, radiating to her back, coming in waves, with severity fluctuating over the subsequent hours. At times she was able to talk and even walk, but her conscious level was mostly reduced, and she experienced difficulty in breathing. She felt dizzy and nauseous. Her mother had survived a type A aortic dissection, 3 years previously, aged 77.

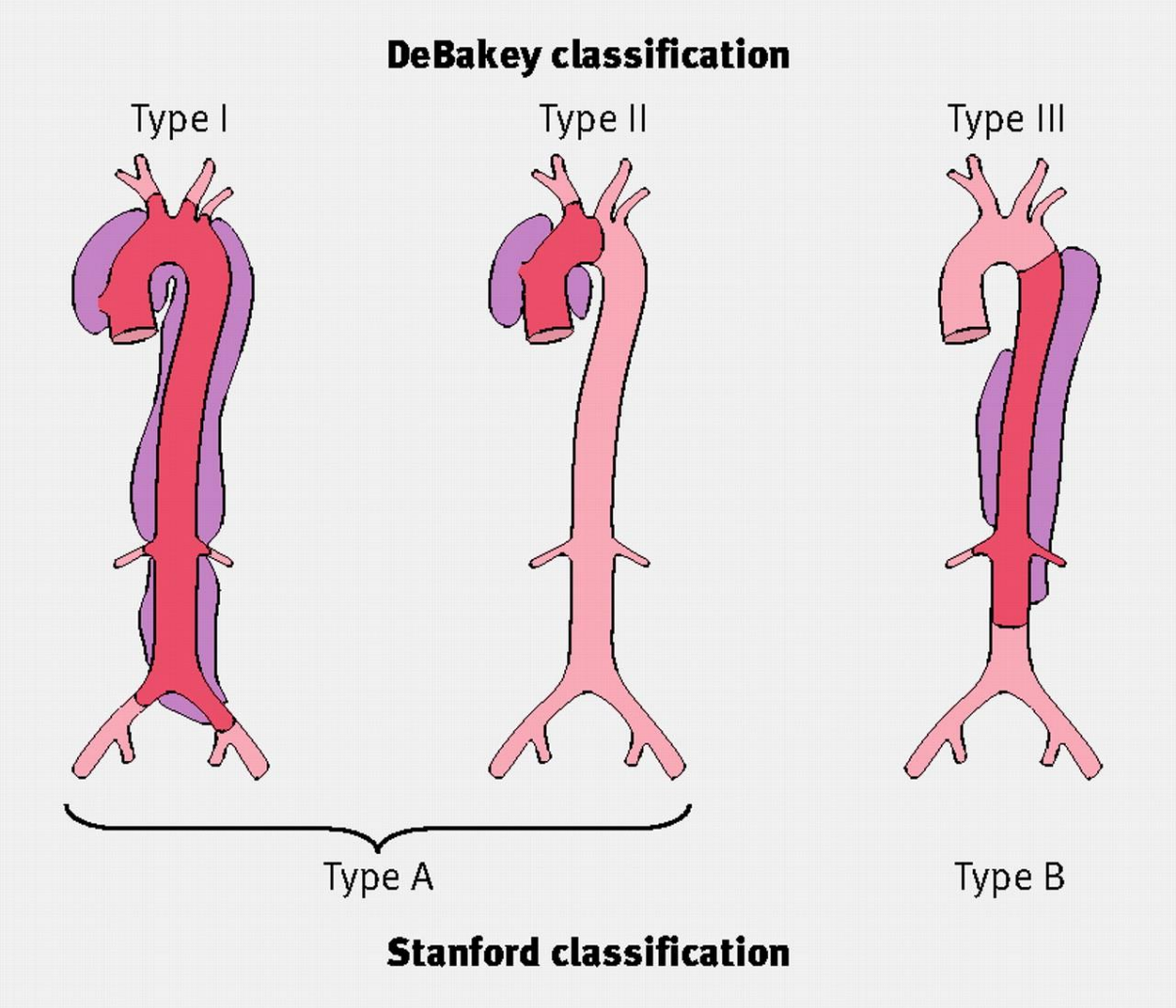
An ambulance was called immediately and arrived 90 minutes later. A paramedic made a tentative diagnosis of aortic dissection based on the presenting features. She was given oral morphine and transported to hospital, arriving 45 minutes later. A panic attack was initially diagnosed in the emergency department, and she was asked to breath in and out of a paper bag. Neurological examination was normal, but she was not examined for a heart murmur or blood pressure difference between her arms. Reassessment by a different clinician six hours after her arrival in the emergency department resulted in CT angiography, which showed an aortic dissection.

The six-hour delay in diagnosis appeared to be due to initial misdiagnosis as a panic attack. This may reflect an ‘anchoring effect’ whereby the clinician fixed on a specific diagnosis and did not appropriately consider information that was inconsistent with their diagnosis. The patient received appropriate treatment once the correct diagnosis was made and has recovered. However, the initial misdiagnosis had a significant psychological effect, prompting concerns about what might have happened if she had been discharged without treatment, and undermined her trust in clinicians.

What is acute aortic syndrome?

Acute aortic syndrome (AAS) is a life-threatening emergency condition involving a tear in the thoracic aorta that can lead to rupture of the aorta and death. It encompasses three conditions: acute aortic dissection, intra-mural haematoma, and penetrating ulcer [1]. It is commonly classified into Stanford type A (involving the ascending aorta) and type B (sparing the ascending aorta) or DeBakey classification, with type 1 involving ascending and descending aorta and type 2 involving ascending aorta alone, as shown in Figure 1. Without treatment, AAS can progress to aortic rupture, with rapid deterioration and death.

Figure 1: Classification of aortic dissection



https://www.bmj.com/content/343/bmj.d4487

How common is it?

AAS is uncommon. Meta-analysis of population-based studies from North America, Europe, Asia and Australasia estimated a pooled incidence of 4.8 per 100,000 individuals/year, with 3.0 per 100,000/year type A and 1.6 per 100,000/year type B aortic dissection [2]. Mean patient age in the studies varied from 58.9 to 77.3 years and the proportion of males varied from 50% to 84%. Hospital episodes statistics for England in 2022-23 reported 1542 admissions with dissection of the aorta out 6 million emergency admissions [3]. Aortic dissection accounts for around three-quarters of AAS [4].

Why is it missed?

AAS is easily missed because the symptoms of possible AAS are also reported by patients with other much more common diagnoses, such as acute coronary syndrome, gastro-oesophageal reflux, and panic attacks. Chest pain is the most common presenting symptom of AAS [5], but was also the chief presenting complaint for 6% of emergency department

attendances in England in 2022-23 [6]. A US retrospective cohort study of 33 emergency departments estimated that one aortic dissection was diagnosed in every 980 attendances with atraumatic chest pain [7]. Low rates of exposure to a diagnosis of AAS may mean that clinicians fail to consider it as a possible diagnosis alongside other more common causes of chest pain. Our case presentation illustrates the diagnosis of AAS being overlooked in the emergency department in favour of a more common diagnosis (panic attack). Emergency physicians see AAS infrequently and a general practitioner may never see a case, but clinicians who assess acute chest pain need to be aware of AAS and how it is investigated to avoid misdiagnosis.

A systematic review of 12 studies (1663 patients) estimated that 1 in 3 patients with an eventual diagnosis of aortic dissection were initially misdiagnosed [8]. The most common misdiagnoses were acute coronary syndrome, stroke, and pulmonary embolism. A more recent estimate from a population-based retrospective cohort study of 1299 patients diagnosed with AAS in Ontario between 2003 and 2018, identified that 13% had attended an emergency department in the previous 14 days with symptoms suggesting AAS [9].

Why does this matter?

Missed diagnosis can lead to delayed surgery for type A aortic dissection and missed opportunities for medical management (blood pressure control) or emergency intervention for type B aortic dissection. Missed diagnosis of type A dissection is associated with an approximate doubling of mortality (hazard ratio 2.14, 95 % confidence interval 0.89–5.13) [10] and delayed surgery is associated with increased mortality (67% at 8-12 hours versus 20% at 0-4 hours after diagnosis) [11]. Blood pressure control using beta-blockers is associated with an approximate halving of mortality in type B dissection [12].

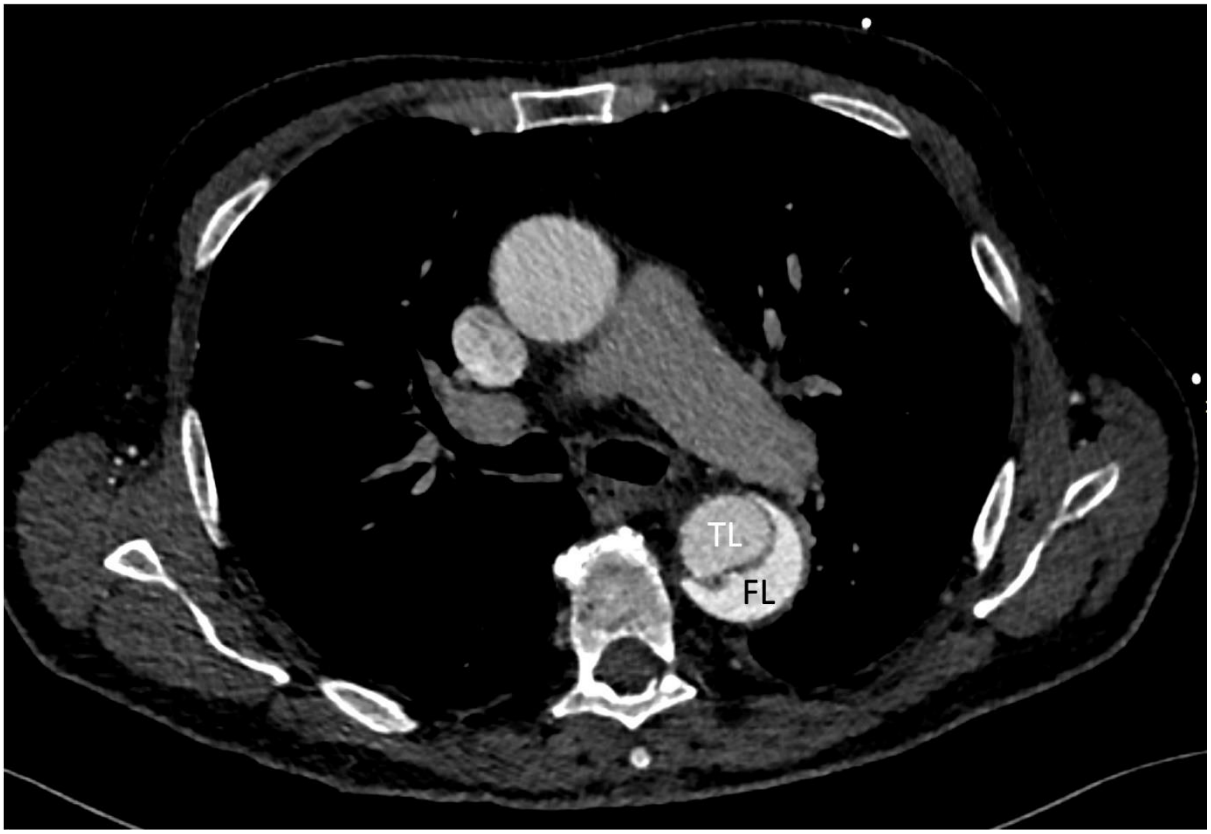
NHS Resolution (an arm's-length body of the United Kingdom Department of Health and Social Care that provides expertise on resolving concerns and disputes) identified aortic disease, including dissection, as a common cause of fatality-related negligence claims [13]. A study of 135 medical practice litigations across the United States involving aortic dissection cited failure to diagnoses as the reason for litigation in 64%.[14] A review by the Healthcare Safety Investigation Branch found that half of patients with acute aortic dissection die before reaching any specialist centre in the UK [15] and a systematic review of fourteen studies of out-of-hospital cardiac arrest identified that the 7% due to aortic dissection had 100% mortality [16]. Data from other countries is sparse but likely to be similar.

How is it diagnosed?

AAS is definitively diagnosed by computed tomographic angiography (CTA) scanning of the aorta (figure 2), or other techniques, such as ECG-gated CTA or magnetic resonance angiography. CTA incurs costs and incurs small risks of radiation-induced malignancy and reaction to contrast media. Clinicians therefore use clinical assessment and biomarkers (if appropriate) to assess AAS risk and select patients for imaging. If the patient is unwell with typical features of AAS and AAS is strongly suspected, then arrange a CTA without delay.

The diagnostic challenge of AAS is well recognized [17] but recent research has clarified the role of clinical assessment and biomarkers. [18-20]

Figure 2: CTA showing aortic dissection with true lumen (TL) and false lumen (FL)



Clinical assessment

Consider risk factors, symptoms, and signs to estimate the probability of AAS. Assessment may be structured, using a clinical score or algorithm, or unstructured, using clinical gestalt. Several scores or algorithms have been developed for AAS but only the Aortic Dissection Detection Risk Score (ADD-RS) has been widely studied [18]. The ADD-RS gives a score

between zero (low risk) and three (high risk) by allocating one point each if the patient has a risk factor for AAS, a symptom suggesting AAS, or a sign of AAS (see table 1).

Table 1: The Aortic Dissection Detection Risk Score (ADD-RS)

High-risk conditions	
• Marfan syndrome • Family history of aortic disease • Known aortic valve disease • Recent aortic manipulation • Known thoracic aortic aneurysm	1 Point if any present
High-risk pain features	
Chest, back, or abdominal pain described as: • Abrupt in onset • Severe in intensity • Ripping or tearing in quality	1 Point if any present
High-risk exam features	
• Pulse deficit or systolic BP differential • Focal neurologic deficit (with pain) • Murmur of aortic insufficiency (new, with pain) • Hypotension or shock state	1 Point if any present

A meta-analysis of eleven cohort studies of the ADD-RS [18] reported that ADD-RS greater than zero had 94.5% sensitivity and 38.3% specificity for AAS, while ADD-RS greater than one had 42.8% sensitivity and 90.2% specificity. The low prevalence of AAS in the clinically relevant population means that sensitivity 95% could be sufficient to rule out AAS, while specificity of 90% is required to avoid over-investigation. These findings could be interpreted as suggesting that patients with an ADD-RS of two or three should be selected for imaging while those with an ADD-RS of zero would not benefit from further testing. It is uncertain how patients with an ADD-RS of one should be managed.

The patient in our case presentation had a high-risk condition (family history) and high-risk pain features, giving a score of two, and indicating the need for CTA. Use of the ADD-RS could also have prompted assessment for high-risk examination findings.

Electrocardiography (ECG)

ECG can diagnose acute coronary syndrome and other causes of acute chest pain but does not assist with diagnosis of AAS.

Blood tests

Blood tests (biomarkers) can be used to select patients with suspected AAS for imaging. D-dimer is the only biomarker that has been extensively studied for diagnosing AAS. Many other biomarkers have had limited evaluation, but none are ready for clinical use [19]. A meta-analysis of 18 cohort studies of D-dimer using a threshold of 500ng/mL reported 96.5% sensitivity and 56.2% specificity for AAS [20]. This is similar to the sensitivity and specificity of D-dimer for diagnosing venous thromboembolism [21] and suggests that D-dimer could rule out AAS in patients with a low or intermediate clinical risk (as determine by the ADD-RS or unstructured assessment), but indiscriminate use in patients with a very low clinical risk of AAS could lead to over-use of CTA. D-dimer sensitivity does not appear to be time-dependent. A cohort study of 273 patients diagnosed with AAS estimated that D-dimer sensitivity was 97% within one hour of symptom onset and did not vary with time from symptom onset [22]. Age-adjusted D-dimer may offer improved specificity compared to a fixed threshold but requires further evaluation.

Transthoracic echocardiography

A systematic review of four studies evaluating emergency physician point-of-care ultrasound for thoracic aortic dissection reported sensitivities ranging from 41% to 91% and specificities of 94% to 100% when an intimal flap was seen [23]. A more recent prospective cohort study (N=1314) of a point-of-care ultrasound protocol combining transthoracic echocardiography with scanning of the abdominal aorta reported 93.2% sensitivity and 90.9% specificity [24]. This suggests a possible role for point-of-care ultrasound in the emergency department diagnosis of AAS, but the role of operator experience needs to be determined. Point-of-care ultrasound is a core skill for emergency physicians, but additional training would be required for diagnosing AAS.

ADD-RS with D-dimer

The ADD-RS has been proposed to be combined with D-dimer in various ways. A recent meta-analysis combined data from six studies of ADD-RS and D-dimer to estimate sensitivities and specificities [18]. Table 2 outlines the sensitivities and specificities of using ADD-RS or D-dimer to select patients for imaging or using each test alone. These provide a range of trade-offs between sensitivity and specificity.

Table 2: Sensitivity and specificity of ADD-RS and D-dimer, alone and in combination

Result(s) indicating a positive test	Sensitivity (95% credible interval)	Specificity (95% credible interval)
ADD-RS>0	94.5% (88.2% to 98%)	38.3% (21.8% to 57.4%)
ADD-RS>1	42.8% (28.1% to 59.4%)	90.2% (80.3% to 95.8%)
D-dimer>500ng/mL	96.5% (94.8% to 98%)	56.2% (48.3% to 63.9%)
ADD RS>0 or D-Dimer>500ng/Ml	99.8% (98.7% to 100%)	21.8% (12.1% to 32.6%)
ADD RS>1 or D-Dimer>500ng/mL	98.3% (94.9% to 99.5%)	51.4% (38.7% to 64.1%)
ADD RS>1 or (ADD RS=1 and D-dimer>500ng/mL)	93.1% (87.1% to 96.3%)	67.1% (54.4% to 77.7%)

When should AAS be suspected?

AAS should be considered in patients with chest, back or abdominal pain, syncope or symptoms related to malperfusion. However, applying diagnostic strategies for AAS to all such patients would result in very high use of CTA. Clinicians therefore need to apply diagnostic strategies selectively to those with a non-negligible risk of AAS, such as those with an additional feature suggesting AAS ('chest pain plus one'). A recent cohort study of 5548 patients attending the emergency department with possible symptoms of AAS found that clinicians rated the likelihood of AAS as zero in 2315/4111 (56%) [25]. Applying diagnostic strategies only to those with a non-zero likelihood of AAS could result in a more deliverable rate of CTA but it is currently unclear how clinicians determine a zero likelihood of AAS and whether this judgement is accurate.

How is it managed?

AAS is managed according to principles set out in the NHS Acute Aortic Dissection toolkit [26], which NHS England produced to improve outcomes from AAS, and international guidelines [5,27,28]. Acute management involves analgesia and reducing systolic blood pressure to 100-120mmHg. Type A AAS is usually managed operatively in a regional aortic centre. Type B AAS is split into complicated or non-complicated by the presence of haemodynamic instability and/or malperfusion of an organ system or limb. Uncomplicated

Type B AAS is usually managed medically with blood pressure control. Although patients may not require transfer to a tertiary centre, they should all be discussed to agree management. Complicated type B AAS may require tertiary transfer for endovascular stent graft placement. In-hospital mortality is 22% for type A and 13% for type B aortic dissection [29].

Future developments

Research into artificial intelligence algorithms [30] and biomarkers may produce new tests to assist with AAS diagnosis, while further evaluation of the ADD-RS, D-dimer and point-of-care ultrasound may clarify their role in AAS diagnosis. This could lead to reduced risk of misdiagnosis and reduced reliance on CTA to rule out AAS.

Box: Guidelines for selecting patients with suspected AAS for CTA

- Royal College of Emergency Medicine and Royal College of Radiologists guidelines [31] recommend CTA if there is no clear alternative diagnosis (such as myocardial infarction, pulmonary embolism, or pneumothorax) and the patient has a high-risk condition, pain feature, or clinical finding for AAS (similar to those in the ADD-RS). https://rcem.ac.uk/wp-content/uploads/2024/01/Diagnosis_of_Thoracic_Aortic_Dissection_RCEM_RCR_v2.pdf
- Canadian clinical practice guidelines [32] recommend clinical probability assessment using risk factors, pain features, examination findings, and alternative diagnosis. Low-risk patients receive no further testing for AAS. Intermediate-risk patients receive D-dimer testing, with CTA if positive and no further testing if negative. High-risk patients receive CTA. https://www.cmaj.ca/content/192/29/E832
- European Society for Cardiology guidelines [5] recommend stratification to high probably (equivalent to ADD-RS 2-3) and low probability (equivalent ADD-RS 0-1) High probability cases are investigated with CTA, low probability with D-dimer, chest x-ray and transthoracic echocardiography. https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Aortic-Diseases
- American Heart Association and American College of Cardiology guidelines [27] state that integrating a low aortic dissection risk score and a low D-dimer may be a useful strategy to exclude the diagnosis of AAS but do not recommend a specific structured strategy. https://www.ahajournals.org/doi/pdf/10.1161/CIR.0000000000001106

Box: Resources for readers

- Royal College of Emergency Medicine learning module on aortic dissection https://www.rcemlearning.co.uk/reference/aortic-dissection
- Royal College of Emergency Medicine / Royal College of Radiologists Best Practice Guideline https://rcem.ac.uk/wp-content/uploads/2024/01/Diagnosis_of_Thoracic_Aortic_Dissection_RCEM_RCR_v2.pdf
- NHS Acute Aortic Dissection Pathway Toolkit https://www.vascularsociety.org.uk/professionals/news/191/the_acute_aortic_dissection_toolkit
- The Aortic Dissection Charitable Trust patient and professional resources https://aorticdissectioncharitabletrust.org/resources/

Box: How this article was made

This article was made using systematic reviews and meta-analysis undertaken for the ASES (Aortic Syndrome Evidence Synthesis) study (see https://fundingawards.nihr.ac.uk/award/NIHR151853), the clinical and personal experience of the authors, and insights from members of The Aortic Dissection Charitable Trust.

Box: How patients were involved in the creation of this article

Valerie Lechene is a patient with experience of AAS. She described her experience of AAS diagnosis (and misdiagnosis) in the case presentation and contributed to writing all elements of this article. She was also a member of the research team for the ASES study that undertook the systematic reviews for this article. The Aortic Dissection Charitable Trust (https://aorticdissectioncharitabletrust.org/) is a charity uniting patients, families, and the medical community in a shared goal of improving diagnosis, increasing survival, and reducing disability due to aortic dissection. Patients and public representatives from the Trust participated in a public involvement group for the ASES study that informed the study design, helped to interpret the findings, and assisted with dissemination of findings through webinars that informed the development of this article.

Box: Education into practice

- What would prompt you to consider AAS in your differential diagnosis for a patient and what factors would increase (or decrease) your suspicion for the diagnosis?
- How would you decide whether to request a CTA for a patient with symptoms that could be compatible with AAS?
- How would you explain the diagnosis to a patient or their family?

Infographic

Aortic Dissection Explained

See: https://aorticdissectioncharitabletrust.org/

Contributorship and the guarantor

SG and GC conceived the idea for the article. SG wrote the initial draft. VL wrote the case presentation based on her experience of AAS. All authors made substantial contributions to the development of the article and revising it critically for important intellectual content. All authors approved the article and agreed to be accountable for all aspects of the work. SG is the guarantor.

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Conflicts of Interest

The BMJ has judged that there are no disqualifying financial ties to commercial companies. The authors declare the following other interests: SG, GC, and SW have received institutional research funding from the National Institute of Health Research to undertake the ASES study. JZ is supported by a Cancer Research UK (CRUK) Clinical Trials Fellowship Grant and has received institutional research funding from The Aortic Dissection Charitable Trust. VL has no conflicts of interest to declare. Further details of The BMJ policy on financial interests is here: https://www.bmj.com/sites/default/files/attachments/resources/2016/03/16-current-bmj-education-coi-form.pdf

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