PRACTICE

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This series of occasional articles provides an update on the best use of key diagnostic tests in the initial investigation of common or important clinical presentations. The series advisers are Steve Atkin, professor, head of department of academic endocrinology, diabetes, and metabolism, Hull York Medical School; and Eric Kilpatrick, honorary professor, department of clinical biochemistry, Hull Royal Infirmary, Hull York Medical School.

RATIONAL TESTING Investigating easy bruising in a child

Julia A M Anderson,¹² Angela E Thomas²³

Differentiating "normal" from "abnormal" bruising in a child depends on careful history taking and appropriate investigations

An eight month old white boy is seen by his general practitioner with a sore throat and a temperature. The GP notes several easily visible bruises on the lateral aspect of his left temple, and on examining his chest notes bruises on his left upper arm and left lumbar region. On questioning, both parents independently state that there is no history of trauma or injury and that the bruises occurred spontaneously over the past two weeks. Both parents are anxious and upset. The GP is concerned about a child with a high fever and bruising, and after discussion with the on-call paediatric registrar the child is referred to the paediatric accident and emergency department.

What is the next investigation?

The investigations to be performed in a child with easy bruising depend on a carefully taken personal and family history to attempt to differentiate "normal" from "abnormal" bruising.¹⁻³ A negative history of bleeding in a young child does not exclude an important bleeding disorder.⁴

History taking

Ask about:

- The mode of delivery and any bruising or bleeding at birth or from the umbilical stump (a classic feature of factor XIII deficiency² and seen in some patients with haemophilia)
- A history of haematoma after routine intramuscular vitamin K given at birth, or of bleeding from the heel prick after the Guthrie test
- A history of epistaxis (rare in the first two years of

LEARNING POINTS

In a child, unusual bruising or bleeding out of proportion to the injury sustained should be investigated after careful history taking and examination, and an open view kept Early discussion with a paediatric haematologist, or adult haematologist with expertise in haemostasis, is essential to ensure optimal investigation with as few venepunctures as possible

All children under investigation for easy bruising or a bleeding tendency should have a full blood count, blood film, and coagulation screen including a thrombin time, in addition to a Von Willebrand factor assay and assays of factors VIII and IX; this is to ensure that mild forms of haemophilia are excluded even if the activated partial thromboplastin time is normal In 30% of cases of haemophilia, there is no family history: it arises secondary to new genetic mutations

life and more often associated with injury or severe illness⁵) or of gingival or mucocutaneous bleeding (suggesting a platelet abnormality or severe Von Willebrand disease)

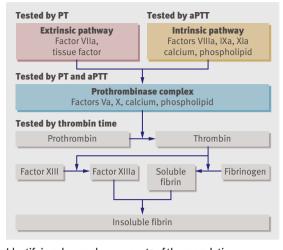
- A history of prolonged bleeding after surgery such as circumcision or tooth extraction
- Any pain or joint swelling or reluctance to move a limb (as seen with haemarthroses)
- The age of onset of bruising, since bruising is uncommon in infants before they crawl⁶
- Unusual bleeding or bruising out of proportion to the injury sustained; this should always be investigated and an open view kept
- Family history of haemophilia, Von Willebrand disease, or platelet function defects (in 30% of cases, haemophilia may arise secondary to new genetic mutations and, as a result, there will be no family history)
- Drug history,⁷ remembering that children may have taken medicines (such as warfarin) accidentally.

In the case presented, the child was born by atraumatic spontaneous vaginal delivery with no noted bruising or bleeding. Intramuscular vitamin K was given without complication, and he had no bruising or bleeding with his vaccinations. He had not had any surgery or previous abnormal haemorrhagic symptoms. His parents had noticed the bruising two weeks before the consultation, which coincided with the start of crawling at home; the child was not obviously reluctant to move any particular limb. There was no history of consanguinity in this family. None of the child's siblings, cousins, or parents had any spontaneous bleeding, although the children had not undergone any dental or surgical challenges.

Examination

When examining a child with bruising it is important to record the distribution, number, site, and size of bruising accurately, along with any petechiae, ecchymoses, and subcutaneous haematoma. Pictorial or photographic records should be made, with parental consent. Note additional signs such as abrasion of the skin or the outline of a hand or implement such as a belt.¹

Check general health and nutritional status, as malnourishment or a limited diet can result in vitamin K deficiency. Vitamin C deficiency can cause perifollicular haemorrhage and bruising but is exceptionally rare. Assess the child's skin elasticity and joint hypermobility clinically, as collagen disorders such as Ehlers-Danlos



Identifying abnormal components of the coagulation cascade. PT = prothrombin time, aPTT = activated partial thromboplastin time

syndrome can cause microvascular haemorrhage.³⁷ In this child, examination was normal apart from the bruises described.

"Normal" bruising in children is common around the age of 1 year, when most children have started "cruising." It is usually restricted to the lower limbs; is not associated with mucosal bleeding, petechiae, or purpura; and the family history is negative. Further investigation is needed in children with an extensive or unusual pattern of bruising over different sites without adequate explanation, a history of excessive bleeding after minor surgical or dental procedures, or a positive family history. A review to exclude non-accidental injury may be necessary for children presenting with an atypical or unusual pattern of bruising (the back, buttocks, arms, and abdomen are uncommon sites for bruising at all ages) and normal haematology test results.³ Bruising carrying the imprint of an implement or hand should always be investigated for non-accidental injury.² In this child, examination was normal apart from the bruises described, and given their unusual distribution (face, trunk, and upper arm), further investigation was deemed necessary when he reached hospital.

Laboratory tests

The first principle to further assess spontaneous bruising is that the haematology laboratory is informed of the case, perhaps by prior discussion with the on-call paediatric haematology registrar or consultant, to ensure the correct and efficient handling of the child's samples and to ascertain the best tests to request initially. As normal ranges of coagulation tests are different in infants, children, and adults, comparison must be in age specific ranges, and a haematologist may be needed to help with interpretation.

Referral to an experienced paediatric phlebotomist may be necessary, as paediatric samples can be difficult to take, are of small volume, and must be appropriately processed to avoid artefact. As these small samples are precious, plasma should undergo double spinning and can be frozen to allow factor assays and investigation of lupus anticoagulant to be performed retrospectively (depending on results of the initial coagulation screening), thus avoiding repeat and multiple venepuncture.

The second principle emphasises the importance of an atraumatic venepuncture to prevent further bruising or haematoma formation should the child have a bleeding disorder, and to prevent activation of the coagulation samples.² Blood taken from a central line can be unreliable because of heparin contamination and should be avoided.² In young children with possible haemostatic defects, blood should not be taken with a vacuum system as this may cause massive haematoma at the puncture site.

The following tests were requested in this child:

- Full blood count (for platelet count and size (mean platelet volume)
- Blood film (for platelet and leucocyte morphology)
- Coagulation screen—prothrombin time (PT) (assessing extrinsic and common clotting pathways, see figure); activated partial thromboplastin time (aPTT) (assessing the intrinsic pathway); Clauss fibrinogen (for fibrinogen function) and thrombin time (for fibrinogen functional defects)
- Assay of Von Willebrand factor (including assays of Von Willebrand factor antigen and function)
- Assays of factors VIII and IX.² Deficiencies of these are the commonest forms of haemophilia and should be assayed in girls as well as boys with appreciable bruising, as female carriers of haemophilia may have low levels of these factors.

These coagulation tests should be possible with a single 1.3 ml (paediatric size) coagulation tube (in addition to the full blood count); ideally two tubes should be taken to ensure that there is enough plasma if further tests are needed, and any spare plasma frozen.

Depending on the laboratory reagents in use, a coagulation screen will identify patients with a deficiency of the extrinsic clotting pathway by prolonged prothrombin time and of the intrinsic pathway by prolonged aPTT (figure). If a 50:50 mix of test and normal plasma corrects a prolonged aPTT, a factor deficiency is present; otherwise an inhibitor of coagulation such as heparin or a lupus anticoagulant is likely to be present. In children, a lupus anticoagulant is usually secondary to infection; it is transient and resolves, but it can cause confusion, as it interferes with the intrinsic pathway in vitro (thus prolonging the aPTT) but not in vivo and is thus not associated with a bleeding tendency. If the aPTT is prolonged and the factor VIII and IX levels are normal, further laboratory tests may be indicative of a lupus anticoagulant, but it is often helpful to assay factors XI and XII as well, to be certain that there is no additional coagulation factor deficiency. Severe immune thrombocytopenia will be indicated by a low platelet count,⁸ and the blood film may show abnormal platelet morphology and other diagnostic features of rarer congenital thrombocytopenias, such as inclusion granules within neutrophils (Chediak-Higashi syndrome).

Further tests after referral to specialist

These tests will identify the major causes of bruising in a child of this age, but results will be normal in

Causes of bruising or bleeding in well children, as indicated by results of full blood count, prothrombin time, and activated partial thromboplastin time¹²¹³

Platelet count normal, prothrombin time (PT) normal, activated partial thromboplastin time (aPTT) normal

Common

Von Willebrand disease Henoch-Schönlein purpura

Uncommon

Platelet function defects (storage pool disorder, Glanzmann's thrombasthenia) Factor XIII deficiency (1:2 000 000 population) Collagen disorders (Ehler-Danlos syndrome, Pseudoxanthoma elasticum) Vitamin C deficiency PAI-1 deficiency (very rare) Ipha 2-antiplasmin deficiency (very rare)

Platelet count normal, PT prolonged; aPTT normal or prolonged

Common

Vitamin K deficiency Warfarin (may cause prolonged PT and aPTT)

Uncommon

Deficiencies of factors II, V, X (deficiencies of factors II, V, X may cause prolonged PT and aPTT)

Factor VII deficiency (1:500 000 population) Afibrinogenaemia (1:1 000 000 population) Dysfibrinogenaemia

Platelet count normal, PT normal, aPTT prolonged

Common

Heparin effect

Haemophilia A (1:5000 male population); haemophilia B (1:25 000 male population)

Uncommon

Factor XI deficiency (1:1 000 000 population; 1:500 Ashkenazi Jewish; a rare congenital coagulopathy, with autosomal inheritance and variable phenotype)

Platelet count abnormal, PT normal, aPTT normal

Common

Immune thrombocytopenia (1:20000 population)

Uncommon

Congenital thrombocytopenias (Bernard-Soulier syndrome, Wiskott-Aldrich syndrome)

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• Mabel Chew interviews the authors of this paper in a *BMJ* podcast available at www.bmj.com/podcasts Glanzmann's thrombasthenia, other platelet function defects, and factor XIII deficiency (see box). The diagnosis of these conditions will require urgent discussion with a paediatric haematologist and specialist referral. In neonates who present with intracranial haemorrhage, or in children with a history of umbilical stump bleeding or delayed bleeding from wounds, factor XIII should be measured⁹; this can be performed retrospectively on the frozen plasma sample, avoiding further venepuncture.

Children with Glanzmann's thrombasthenia tend to present with a severe clinical picture of bleeding, including bleeding at birth, fingertip bruising, and bleeding from vaccination sites. The diagnosis is made by platelet function testing.

Determining bleeding time in a newborn or toddler should be avoided. It is technically difficult, stressful for the child, and often unhelpful, as results can show considerable intra-observer and inter-observer variability. Platelet function testing is preferred but requires comparatively large amounts of blood. Targeted testing can reduce the amount of blood required. The findings may be difficult to interpret, especially if minor abnormalities are shown. It is important to exclude Glanzmann's thrombasthenia if the clinical history is suggestive; this can also be done by flow cytometry¹⁰ or with an automated platelet function analyser, which can exclude Glanzmann's thrombasthenia but not other milder platelet disorders.¹¹

Outcome

For this child, the full blood count and blood film were normal, excluding immune thrombocytopenia and bone marrow failure syndromes, but the aPTT was prolonged at 82 seconds; it corrected to 45 seconds with a 50:50 plasma mix, indicating an underlying coagulation factor deficiency. Assays for factor IX and Von Willebrand factor were normal, but factor VIII assay was only 0.01 IU/ml (1%), indicating an underlying diagnosis of severe haemophilia A.

Management options include treating any acute bleeds with a concentrate of factor VIII; in the United Kingdom, recombinant factor VIII products are used. Prophylaxis regimens are also used to minimise long term damage to joints. The child remains under the direct care of a paediatric haematologist, is registered at a haemophilia comprehensive care centre, and has been issued with a haemorrhagic states card outlining his condition and giving contact numbers for emergency advice if required.

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A PATIENT'S JOURNEY Through and beyond anaesthesia awareness

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This is one of a series of occasional articles by patients about their experiences that offer lessons to doctors. The *BMJ* welcomes contributions to the series. Please contact Peter Lapsley (plapsley@bmj.com) for guidance. For this patient the general anaesthetic for her emergency caesarean section failed and she remained awake during the procedure

On the morning of 2 January 2004, I gave birth to my second son when I was less than 26 weeks pregnant. The delivery was by emergency caesarean because the umbilical cord had prolapsed, cutting off the blood and oxygen supply to my tiny baby. It was a shock to realise that my son was in grave danger, but I was very thankful to the healthcare staff for responding immediately and doing their utmost to save his life.

Because of the acuteness of the situation, the caesarean was to be carried out under general anaesthesia. Frankly, this was a relief—I was terrified my son might already have died and, therefore, preferred not to witness him being delivered. I had been under general anaesthesia before without any problems and was not too anxious about going through it again.

The experience itself

Unfortunately, something went terribly wrong. The drug that should have put me to sleep worked only partially, but nobody registered this. Instead, the anaesthetists proceeded to give me a muscle relaxant. I was partly drugged, which made me forget the context: that I was giving birth through a caesarean. Otherwise, however, I was wide awake, with no soothing effect of painkillers. I experienced how my muscles twitched then became totally paralysed so I could not breathe, and how a flat metal blade that felt like a knife was put into my mouth and jammed down my throat, followed by a thick wire-like thing that I thought further obstructed my breathing. I then felt an arm being thrust into my vagina (this was to keep my child from advancing into the pelvis, but felt as if I was being raped) and the cool feeling of liquid on my tummy, followed by agony when the obstetrician cut my abdomen open. Because I had forgotten about the caesarean, I thought that I was being raped, strangled, and cut up by some evil force. For a few seconds, I would black out in terror, then wake up again, only to realise that I was dying and unable to fight for my life.

After a few minutes my son was delivered, which was when I received a large dose of opioids and finally drifted away, not realising that I had just become a mother for the second time.

The months after

When I woke after the anaesthesia to learn that my child weighed only 751 g but had survived, I remembered none of the dramatic events surrounding his birth; I was in control and acted rationally. The next few days, however, I reacted very strongly. I cried and was terribly frightened without understanding why. Everybody, including my husband and myself, believed that it was because I was afraid my son would die, which made perfect sense because he was seriously ill. When his condition ultimately improved and he was discharged to go home, my symptoms failed to cease.

During the first few months after his birth, the recollection of how my son was delivered slowly re-emerged as nightmares and uncontrollable flashbacks. I would wake in the middle of the night scared to death about choking, with the memory of a sharp, shiny metal thing being thrust into my throat without me being able to lift a finger to defend myself, or with a strong impulse to vomit or an urge to pee, without any physical cause.

To start with, I refused to relate my nightmares to the anaesthesia—they were too horrifyingly brutal to be true. I finally told first my husband (more than six months later, when my son had stabilised), then my general practitioner about the nightmares. They suggested that there might be a link with the anaesthesia, so I contacted the hospital where my son was born to arrange a meeting with the anaesthetist who had taken care of the anaesthetic on that morning.

Coming to terms with the experience

Meeting the anaesthetist was a scary experience because the anaesthetic drugs had made me lose the context of what was happening. Emotionally, the person I was meeting represented those people who had conspired to rape, strangle, and kill me that morning, and I had spent some time before the meeting being very angry and wishing to avenge what had happened to me. My husband commented that my experience must be similar to that of a torture victim, and that being horrified was a very understandable reaction. Nonetheless, I shook with fear when I finally sat opposite the doctor who had anaesthetised me. At the same time, my rational self realised that she had not intentionally hurt me, and that I needed her help to understand what had happened.

During the following six months, I met with the anaesthetist on a regular basis, underwent therapy from a

Things that helped me get over my awareness experience

1) My family, friends, and, not least, my doctors listening to me and believing in me

2) People understanding that even though I had not undergone torture or an attempted killing, this was how I had perceived the anaesthesia and surgery

3) The anaesthetist explaining the technicalities of my experience to me and teaching me how to intubate. And finally learning to trust her enough to let her hold my head again and help me to lie on the operating table again

4) The anaesthetist telling me that my experience was intolerable and unacceptable from a professional point of view, and apologising for it

5) A psychologist helping me work through my experience

A DOCTOR'S PERSPECTIVE

When I first heard of Anne-Marie's experience, some ten months after the event, I had no problem remembering what had happened on the morning in question or accepting that she had suffered an awareness experience. Then, I was an anaesthesia trainee with about four years' experience.

Two other experienced anaesthetists had been present at the scene: a specialist anaesthesiologist and a nurse anaesthetist. We had been working a long, busy shift, and the pager calling us to Anne-Marie's case went off ten minutes before hand over. A general anaesthetic was planned because of the urgency and the risk that the baby might have died in utero.

Several things went wrong, however, which was annoying to us but might have added to Anne-Marie's suffering. The anaesthesia apparatus repeatedly failed the electronic self test, which precluded us from using sevoflurane (an inhalation anaesthetic); instead, we decided to use propofol to maintain the anaesthesia. Next, after the usual crash induction sequence of thiopental sodium and suxamethonium chloride, which we thought had put Anne-Marie to sleep, I intubated the oesophagus instead of the trachea. Although we realised and corrected the error immediately, I have no doubt that the sensation of air deprivation, as well as being intubated twice, aggravated the nightmare that Anne-Marie was experiencing. Additionally, the peripheral intravenous catheter supplying the propofol infusion was displaced during the induction and had to be replaced.

My previous understanding of anaesthesia awareness was thorough but theoretical—I knew that it happens for one to two individuals out of a thousand people undergoing anaesthesia; that the risk can be especially high in women who undergo general anaesthesia for emergency caesarean; and that severity can vary from a vague recall of intraoperative events to catastrophic, agonising post-traumatic distress syndrome.

psychologist, and addressed my emotions from the awareness experience. The anaesthetist explained how my nightmares were related to the events that had taken place when I was anaesthetised and underwent surgery. Understanding what had happened helped me a lot, and I slowly learnt not to be afraid of the anaesthetist. She taught me how to intubate a resuscitation manikin, which helped me work through my own memories of being paralysed and intubated. After half a year of therapy, I voluntarily entered the operating theatre again, lay on the operating table, and let the anaesthetist stand behind me and hold my head. That was a proud and exhilarating moment.

The anaesthetist had also been affected by my awareness experience, but our meetings helped us both to get over the event. I know that several of her colleagues advised her to stop seeing me, but she continued even though it was tough for her. In some ways, my role in our mutual experience was less complicated than hers—I was the injured party, which earned me sympathy and support from people around me, whereas she was the one who was responsible for my suffering, even though it had been impossible to detect during the anaesthesia.

Finding closure

I have learnt a lot from my awareness experience. First of all, I have learnt how strong you can be when you have something very important to fight for. During the first months after my son's birth, I had my premature baby to fight for, and I did that very well. I also learnt that it is important to ask for help if

However, to my knowledge I had never before anaesthetised a patient who subsequently turned out to have been aware during the procedure. Hence, I had no idea of the extent of the suffering that Anne-Marie had been through and was unprepared for the shock that it was to meet with her.

As a doctor, I have been taught skills that are supposed to help others, so I found it deeply distressing to learn how Anne-Marie had perceived me as a cold blooded, evil torturer and murderer. Professionally, I had second thoughts about my choice of specialty and considered resigning from my anaesthesia residency. Personally, I developed post-traumatic distress syndrome, which was nothing like as severe as what Anne-Marie had been through but was nonetheless quite painful. Some of my colleagues questioned my approach and suggested that I pull out of the contact with Anne-Marie to protect myself, which sounded very appealing. On the other hand, I had promised to help her out, and, curiously, working together provided a "cure" for both of us.

Like Anne-Marie, I have learnt a lot from this incident, first and foremost about the potentially traumatising personal consequences that an awareness experience might have. I also got a taste of what post-traumatic distress syndrome is like, on a small scale. Moreover, I was forced to reflect on my obligation as a doctor to assume responsibility, and I realised that I had to make my own moral choices.

Finally, Anne-Marie helped me as much as I helped her. Maybe it would have been more "professional" of me not to get as deeply involved as I did, and others might find that our approach won't work for them. Even so, today I am sure that Anne-Marie and I found the optimal solution for our mutual problem.

Kirsten Møller, specialist in anaesthesiology and intensive care

you cannot handle a problem yourself, and I've learnt about trusting somebody again and forgiveness. I am less afraid to die because I believe that dying will be a lot less painful and terrifying than being killed slowly on an operating table. I am also now open to the possibility that a person might need to die simply because they are suffering so much that life becomes worthless.

The anaesthetist and I have become friends, and we still see each other six years after I thought that she was going to kill me. Today, I would trust her with my life without hesitation. I consider myself 95% cured from the severe post-traumatic stress disorder I experienced. I have returned to work as a psychologist and am doing well. I have written a book about having a premature baby, published a few months ago, that includes a description of the awareness experience. It helped me a lot to write it all down. My husband and friends think I have changed, mostly in a positive direction. I personally feel that I have grown less able to sense my emotions; fortunately, I strongly sense my love for my family and my gratitude to all those who helped me heal.

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