QUESTIONS AND ANSWERS FOR PARENTS OF CHILDREN WITH ACHALASIA

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With Dr Osvaldo Borrelli, consultant paediatric gastroenterologist, Great Ormond Street hospital, London, and Dr Raj Parmar, consultant paediatric gastroenterologist at Great North Children’s hospital, Newcastle upon Tyne. Chaired by Majid Hashemi FRCS, Medical Chair, Consultant Upper GI Surgeon. (The questions were mostly sent through in advance).

• Why is it so difficult to understand what causes achalasia?

It is difficult to analyse the details of what is happening to the cells of the oesophagus because it is a very delicate organ and one cannot risk puncturing it by trying to remove a full thickness sample for biopsy / histological examination, as is possible with some other parts of the body. Achalasia involves the nerve endings of the muscles that control peristalsis (the muscle action that propels food down to the stomach). Sometimes there may be a genetic predisposition. There is sometimes a link with a virus or infection like chicken pox, the varicella zoster virus, or Chagas disease (in Mexico). Some people have suggested it is an auto-immune disease where antibodies work against the nerve system. In animal studies there has been found to be an inflammatory response, and a link to HLA genes that regulate the immune system in humans.

It is also a rare condition and even rarer for children. A study from Chelsea & Westminster looked at 228 child patients for the period 1998-2008. The UK incidence (number of children diagnosed each year) was 0.1 diagnosed per 100,000 (1-2 in a million children) and the prevalence (number of people affected overall) roughly the same.

<table>
<thead>
<tr>
<th>Region</th>
<th>Mid-2003 population 2003 (under 16)</th>
<th>Cases (n)</th>
<th>Mean incidence (cases/10^6 children/year)</th>
<th>95% confidence limits for incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>11712200</td>
<td>228</td>
<td>0.18</td>
<td>0.15 to 0.2</td>
</tr>
<tr>
<td>England</td>
<td>9803500</td>
<td>193</td>
<td>0.18</td>
<td>0.15 to 0.21</td>
</tr>
<tr>
<td>Scotland</td>
<td>943200</td>
<td>25</td>
<td>0.24</td>
<td>0.15 to 0.36</td>
</tr>
<tr>
<td>Wales</td>
<td>577300</td>
<td>7</td>
<td>0.11</td>
<td>0.04 to 0.23</td>
</tr>
<tr>
<td>Northern Ireland</td>
<td>383100</td>
<td>3</td>
<td>0.07</td>
<td>0.01 to 0.21</td>
</tr>
</tbody>
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Marlaiset al Arch Dis Child 2011;96:192–194
A study in Amsterdam confirmed this level of rarity. There had been 87 patients under 18 years of age at eight academic centres 1990 – 2013 in the Netherlands. Mean incidence from 1990 to 2012 was 0.1/100,000 (range 0.03/100 000-0.21/100 000) children/ year, and prevalence in 2012 0.9 per 100,000 children (Smits et al. JPediatr 2015).

Number of cases of childhood achalasia diagnosed in the UK each year:
At Great Ormond Street (GOSH), they see only one or two children under 16 years with achalasia in a year, equivalent to 1 in 500,000. The increase in diagnosis of children over a decade was perhaps because paediatric gastroenterology has been organised in more specialised tertiary (specialist) hospitals that has improved the diagnosis process.

Sometimes high resolution manometry (a test that measures the muscle pressure all the way down the oesophagus when something is swallowed) has been able to diagnose achalasia where the barium swallow tests (a white liquid swallowed whilst the child is monitored with x-ray) were inconclusive. At GOSH they can do manometry on children as young as a few months old, using a much thinner catheter tube. Sometimes a small amount of anaesthetic is used in the child’s nostrils to help place the manometry tube. GOSH do a barium meal study, and endoscopy followed by manometry. The manometry is conducted when the child is fully awake after sedation, so that the sedative does not affect the results. As with adults, an endoscopy in itself tends not to detect achalasia (but food residue might be noted) and is often reported as ‘normal’; the achalasia diagnosis most often relies on barium swallow and manometry. But an endoscopy is necessary to check on whether there is some form of physical obstruction causing swallowing difficulty.

The children are often referred with difficulty in swallowing, vomiting or refusing solid food. GOSH is unusual because it has a specialised neuro-gastroenterology centre that looks at motility (process of food progressing through the digestive system) issues. Sometimes children have been initially treated for reflux elsewhere and are referred for specialist examination because the reflux treatment has not been as successful as expected. Sometimes their symptoms have initially been seen as a behaviour problem such as refusing food, or as an issue such as anorexia.

<table>
<thead>
<tr>
<th>Chief complaints in childhood achalasia</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regurgitation/Vomiting</td>
<td>80</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>76</td>
</tr>
<tr>
<td>Loss of body weight</td>
<td>61</td>
</tr>
<tr>
<td>Respiratory tract symptoms</td>
<td>44</td>
</tr>
<tr>
<td>Thoracic pain</td>
<td>38</td>
</tr>
<tr>
<td>Faltering growth</td>
<td>31</td>
</tr>
<tr>
<td>Regurgitation at nighttime</td>
<td>21</td>
</tr>
</tbody>
</table>

• How is children’s achalasia different from adults’?

Doctors do not see ‘end stage’ (when the oesophagus becomes very distorted over time) achalasia with children because the condition has not been present for long enough. Children do present with pneumonia more often than adults because their oesophagus is shorter and therefore it is easier for regurgitated food to reach the lungs. The manometry characteristics are very similar to those for adults.

• Are there any books or videos available to help explain to a young child’s school friends why she is ‘sick’ a lot?

No. But it would be a good idea to produce something. Dr Borrelli complimented the Achalasia Action booklet *A Patient’s Guide to Achalasia*. [This can be downloaded from our website www.achalasia-action.org/information-hub.html][1] There is also an animated video in the course of production that should be available later in 2021.]

• If achalasia is an auto-immune disease, could this be the reason why our 4-year-old seems to have such trouble fighting infections like a cold, ‘flu or a cut head?

There may be cases of achalasia that may be associated with auto-immune disease or occur in patients who have such a disease. As far as we understand it, this is not of the scale of some other conditions which are actually autoimmune in aetiology (how they are caused) and where for instance, treatment would entail prescribing immune-suppressant drugs or steroids.

Essentially, achalasia is not an auto-immune disease in that sense so it would not have caused difficulty in combating infections as described in the question. A study in Belgium on mice did show significant inflammatory infiltrate and possible damage to nerves triggered by infection, but this was very experimental.

• From a 9-year-old ‘Why is it easier to eat and swallow processed foods rather than healthy foods?

You can put healthy food through a blender and have pureed food. It needs to be moist, soft and fluid to help it to get through to the stomach. Honey can help. Some high fibre food can be in liquid form. Very young children often understand the types of food that will cause problems and understandably want to defend themselves from eating them. They can be good at home with parents, but when they are adolescents, things can slip when they are eating out with their friends.

• Diet – how to maintain nutritional intake and ensure eating is relaxed and enjoyable (for a 4-year-old)?

• Other than children’s milkshake supplements are there any other recommendations to help make sure children are receiving vital nutrition?

Milk shakes can be very good at maintaining nutrition. It is important to look at the child overall and see whether they are gaining a proper weight and have the right level of nutrition. But if there is a problem there are not many other options. [Some healthy foods can be mixed with ice cream, jelly or other food that the child likes]

• Any advice on protection from rapid tooth decay as the result of this condition for a 9-year-old?

There can be higher levels of acid and this can affect the enamel on teeth. Sometimes delaying cleaning the teeth can be helpful as the acid level drops away after eating. If the problem is caused
by reflux that comes from the stomach itself, there is the possibility of using PPI medication to reduce acid production, or Gaviscon. If it is from food residue left in the oesophagus it is more difficult to combat. Tooth decay can be the warning sign that leads on to a diagnosis of reflux and/or achalasia. Seeing a dentist would be prudent.

- **Spasms. Can regurgitation in a 4-year-old be caused by spasms themselves rather than the nature / effect of the food?**

  Spasms do not cause regurgitation directly. The spasms are triggered off by a variety of causes, including food, and when food gets stuck. The nature of food and its texture can cause problems, for instance white bread, white rice, red meat and so on. Spasms can be treated with Buscopan, calcium channel blockers or nitrates but this is not always successful. The way the oesophagus contracts can cause spasms.

- **Why do even problem foods sometimes *not* cause regurgitation?**

  It is frustratingly normal for people to experience good days and bad days without a consistent pattern, for reasons that are unclear.

- **Can prolonged regurgitation cause damage to the oesophagus?**

  Food getting stuck and lying in the oesophagus can have a long-term effect such as Barrett’s Oesophagus [where the cells of the lining of the oesophagus start to change, without causing a problem in itself, but potentially developing dysplasia, an enhanced cancer risk]. This would not affect people in their childhood as it would take years to develop.

- **POEM and Heller’s Myotomy. Is it best to delay invasive procedures, or to undertake these early: what age for children is best?**

  If a definite and clear diagnosis has been reached, it is best to go ahead with definitive treatment. The age itself should not normally be a limiting factor. Steps can be taken to make the experience less distressing for the child. Some types of achalasia respond better to POEM; some to Heller’s myotomy (HM). If the manometry indicates significant spasms, it tends to be treated at GOSH with POEM. There are no data about comparing POEM and HM head-to-head, and not all medical colleagues agree on the comparison. The length of the myotomy can be very important. POEM can tend to involve cutting longer lengths of the muscles, and some HM are shorter. In adults, Majid Hashemi aims for a minimum 10 cm length, 3-4 cms of which is within the stomach itself, and he does an endoscopy in the theatre immediately before and at the end of the surgery to check the effectiveness of the procedure.

- **Does the oesophagus get bigger and improve in adulthood?**

  The oesophagus does grow longer as the child grows. The oesophagus can tend to get unhealthily wider over time if the achalasia is not treated because of the pressure of the accumulating food resting there. The condition of achalasia in itself does not generally improve over time unless it is treated.

- **Can a 9-year-old boy who has already had a Heller’s myotomy / fundoplication redone have further revision when he becomes an adult?**

  Yes, this can be done, and Majid Hashemi has performed these operations successfully. GOSH transfer their patients to University College Hospital when they reach 16 years of age. The fundoplication (the top of the stomach being partially wrapped round the base of the oesophagus to
POEM is a procedure that allows an endoscope to be inserted through the mouth and throat and to cut the muscles within the wall of the oesophagus rather than having a keyhole surgery (Heller’s myotomy). It would need proper investigation to try and find out why regurgitation, or reflux, is occurring. It might be a question of prescribing PPI anti-reflux medication (like Omeprazole, which cuts the production of stomach acid). A POEM procedure can be repeated. The individual case involved an experienced doctor who did only a 4 cm length POEM because he was concerned about reflux, and advised that a future dilatation would be appropriate. With children, the POEM length is typically 7-8cms. The rationale of the original doctor was acknowledged as 20-25% of POEM procedures do result in some reflux afterwards. Reflux could be treated with PPI medication, but this might be lifelong. A balloon dilatation is possible after a POEM and before a second POEM. It is sometimes appropriate to wait to see how the child gains weight before making a decision, and to see what happens if the child gets on with, say, trying to drink more water. It is difficult to make an individual judgement from formal clinical studies when the number of children who suffer from achalasia is so small.

**Suffering from heartburn / reflux especially at night, and food blockage for a 14-year-old two years after an otherwise successful Heller myotomy and Dor fundoplication. Could this be an internal change? Does this justify a follow-up consultation despite COVID?**

A Dor fundoplication is one of a variety of techniques that vary according to how far the stomach fundus is wrapped around the oesophagus. It certainly 100% needs another consultation. The National Health Service is still open despite COVID. The heartburn / reflux might be treated with medication, but an endoscopy would be a good idea to investigate the reason for the blockage, any oesophagitis and perhaps further tests like barium swallow and manometry as well. Majid Hashemi follows adults up after HM to check for reflux because of the effect on quality of life, and has sometimes adjusted the fundoplication wrap rather than revising the myotomy, with a number of successful interventions.

**Request for an update on stem cell research**

Professor Paolo de Coppi has been working on this issue for some years, and hopefully in the next 5-10 years there might be significant progress. In test tubes there has been success in growing a neural network from stem cells. Achalasia should be a good model for this. [Conor McCann, who studied stem cell treatment had been awarded a Derek Butler Fellowship by GUTS UK charity, which ended in December 2020, but he retains an interest in achalasia. He has been awarded further funding to examine different potential sources of regenerative cells for enteric nervous system diseases (via the Medical Research Council) and to examine the effects of transplantation on gut tissue elsewhere in the digestive tract].

**Acupressure / acupuncture has been helpful on an individual basis, but is there any more formal research to verify this?**
There was no definite experience or knowledge about this, but a good number of patients do find complementary medicine techniques helpful, and in those cases it is good to see an improvement in their quality of life. Relaxation techniques are observed to be helpful, and patients do find a number of coping strategies. Stress does appear to make swallowing worse.

- **How often do HM fundoplication wraps develop complications afterwards as the child grows?**

Majid Hashemi had not experienced many problems with this in adults as the patients he took on from GOSH were normally fine. He was careful to monitor patients for reflux and the wrap could be adjusted surgically if necessary. Sometimes the wrap does loosen. The wrap is designed to be relatively loose to allow for better swallowing.

- **Can an HM be repeated?**

Yes it can be repeated but more than one revision becomes very much more difficult and should not really happen. There is a difference between revising the myotomy (the cutting of the muscle), which can be more difficult, and separate from revising the fundoplication wrap, which can be done with keyhole surgery. More than one revision may involve cardioplasty (repair of part of the stomach) which would result in a very wide lower oesophageal sphincter and a considerable reflux issue.

- **What is the best test for reflux after POEM?**

The 24-hour pH impedance test can be used; the 48-hour Bravo pH test is best. You can have two situations, one being reflux of stomach contents; the other being acidity from the stasis, or blocked fermenting food, inside the oesophagus itself, each a distinctly different problem. If it is not reflux you may have a continuing baseline of acidity.

- **Can gluten-free food be an issue?**

Gluten-free food is appropriate for a child of any age, but the issue is to find out whether or why the child has the intolerance, or coeliac disease. That will affect the food that is beneficial for them, and there will be additional concerns to make sure that the texture and softness of the diet is also consistent with the achalasia issues. For the individual child about whom the question was raised it appears that a POEM had been performed and swallowing was much improved.

- **Does the angle of HIS affect reflux?**

Yes, the angle of HIS (the angle at which the oesophagus joins the stomach) can be an important factor for reflux.

- **Is there a problem for balloon dilatations in a child of a few months of age?**

At GOSH there is special expertise for doing dilatations when a child is only a few weeks or months old when there is oesophageal atresia (narrowing of the oesophagus), and these procedures often result in much improvement. For adults, myotomy surgery it is always easier when there has not been a history of multiple dilatations, but there are also cases where dilatations can be very effective in helping a child or young person to improve their quality of life through their years of growth and education and when they can become psychologically happy about their eating. This can be helpful in delaying the point when they have to make a decision about a longer-term solution such as HM.
• What is the best period for follow up appointments?

For adults, follow up periods, especially involving a repeat endoscopy or barium swallow test, vary enormously, and there is no real consensus amongst specialists. Majid Hashemi conducts a review 12 months after a Heller’s myotomy for patients who are well and without significant symptoms. Some medical papers refer to repeat imaging every three years, but this could be excessive for somebody without problems.

After a POEM the first review and check for acid reflux would be after one year because the incidence of reflux afterwards is quite high. There may be oesophagitis that has developed, but after that it depends on each child’s situation, and a review would be, say, every three or four years, on an individual basis, dependent upon the symptoms experienced. In the current situation, COVID has delayed many such appointments.

• What can be done for my child’s painful, incapacitating and exhausting spasms?

A low dose of calcium antagonist medication or nitrate is sometimes prescribed to children with the dosage being reviewed and sometimes increased. This is sometimes given between the time of diagnosis and when treatment such as a dilatation is performed. Sometimes this is successful.

Management of pain is important, because stress can reinforce the pain and spasms. For the child about whom this question was asked, who had already had a dilatation and a POEM, further investigation would be appropriate to check whether the POEM has been effective. Muscle pressure in the lower oesophageal sphincter might still be too high, causing the spasms, but there should be a further investigation to try and find the cause of the spasms. When the spasms are significantly frequent and intense it does justify further investigation. Although people may be reluctant to undergo manometry it is really the most effective test to analyse where the problems are occurring and to tailor the best treatment for the individual child. Children tend to appreciate the importance of the tests and are often wonderfully cooperative during the tests, notwithstanding the understandable anxiety of parents. Children and young people should not be given invasive procedures without the best possible investigation of why their problems are occurring, and manometry is the best means for revealing the problems.