Gastrointestinal problems in individuals with CdLS

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The bearer of this card has 
CORNELIA DE LANGE SYNDROME a 
condition that may cause the following: 

A. Growth and Endocrine Problems 
B. Gastro-intestinal problems 
C. Seizures 
D. Cardiac problems 
E. Neurological, learning and 
   behavioural problems 
F. Oro-dental problems
Health Professional Information for Cornelia de Lange Syndrome (CdLS) [Brachman-de Lange Syndrome]

CdLS is a rare, usually sporadic, dysmorphological syndrome with a birth incidence of between 1 in 40,000 and 1 in 100,000. The diagnosis is clinical and usually based on the combination of distinctive facial appearance, limb anomalies and prenatal onset short stature. Many diagnoses are not uncommon and this care card assumes that a firm diagnosis of CdLS has been made by an experienced dysmorphologist. The aim is to highlight treatable complications of the disorder and to provide a record for health professionals of all clinicians involved with each patient.

Growth and Endocrine Problems:
Almost all children with CdLS show both pre and postnatal growth failure in spite of adequate intake. The use of specific CdLS growth charts is strongly recommended and these are available at no cost on-line at [http://www.cdls.org.uk/background]. Therapy with recombinant growth hormone is generally considered non-essential. Cryptorchidism and micropenis are relatively common in males. Puberty can be slightly delayed in both sexes but may be incomplete. Primary amenorrhoea is common.

Gastrointestinal Problems:
Gastro-oesophageal reflux disease (GORD) is very common and under-recognised. Undiagnosed GORD may be an explanation for behavioural abnormalities, pain, soft stools, recurrent respiratory disease or other gastrointestinal symptoms and signs. Many children benefit from endoscopy and/or a therapeutic trial of medication such as a proton pump inhibitor. Fundoplication may be required. Barrett’s oesophagus and Sandifft complex can occur. A low threshold for referral to a paediatric GI specialist is recommended. Acute surgical presentation may be due to caecal volvulus and malrotation of the caecum and ascending colon. Diaphragmatic hernia, duodenal atresia and annular pancreas are also non-randomly associated with CdLS.

Ophthalmology and Audiology:
Ptosis, recurrent blepharocconjunctivitis and strabismus are common in CdLS. Ptosis surgery may be useful in motor development. Baby shampoo or eye drops may be helpful in relieving recurrent red eye discharge although some children may require nocturnal duct probing for obstruction. Nystagmus, mild microcornea, and dislocation of the lenses can occur. Cataract and glaucoma can also be seen. An unusual feature is a small optic disc and slight ptosis. Hearing loss is very common and assessment by a paediatric audiologist is recommended. External ear canal stenosis is very common.

Cardiac Problems:
Congenital heart disease has been reported in 20% of cases, usually ventricular septal defects or pulmonary artery stenosis. Pericardial thickening is very common and may not, at present, require further investigation.

Dermatology:
Cutis marmorata and generalised hirsutism are very common features of CdLS and do not merit further investigation.
Reflux and GERD

Medical Professional Resources

Pediatric GERD Resources for Medical Professionals

CDHNF is pleased to provide professional education resources on pediatric reflux and GERD for medical professionals. If you are interested in conducting research on this condition, please consult our research grant opportunities. For additional information to share with your patients, consult our parent and patient resources for reflux and GERD in infants and GERD in teens.

Education for Quality Improvement for Pediatric Course on GERD

(View Flash Demo)

Clinical Guidelines

NASPGHAN Guidelines for Evaluation and Treatment of Gastroesophageal Reflux in Infants and Children
Major problems

• Gastro-oesophageal reflux and GORD
• Swallowing problems and choking
• Gassiness
• Constipation
• Diarrhoea
• Nutritional issues
• Surgical issues
• Thinking outside the box!
Reflux in children….mostly physiological (normal)
Prevalence of GOR(D) in the ‘normal population’

• **GOR**
  - 50% infants < 3/12
  - 5% of 10-12 month olds  
    Nelson SP, Arch Pediatr Adolesc Med 1997

• **GORD - pathological**
  - Heartburn, regurgitation, dysphagia
    GORD symptoms in 33% of 14 -18 year olds
    smoking and alcohol
    Ramesh P, NASPGHAN Orlando 2001

• **US adults at least 20% GORD prevalence**
Presenting Symptoms and Signs of GORD

- Recurrent vomiting in infant
- Recurrent vomiting and poor weight gain in infant
- Recurrent vomiting and irritability in infant
- Feeding refusal
- Recurrent vomiting in older child
- Heartburn in child/adolescent
- Oesophagitis
- Dysphagia and choking
- Breathing problems or ALTE
- Asthma
- Recurrent chest infections
- Upper airway symptoms
- Abnormal posturing
- Abnormal behaviour
- Self Injury / harm
Pathogenic Factors in GORD

Mechanisms of GOR
- Transient LOS relaxation
- ↑ Intra-abdominal pressure
- Reduced esophageal capacitance
- ↓ Gastric compliance
- Delayed gastric emptying

Mechanisms of Esophageal Complications
- Impaired oesophageal clearance
- Defective tissue resistance
- Noxious composition of refluxate

Mechanisms of Airway Complications
- Vagal reflexes
- Impaired airway protection
GOR Complications

Oesophageal stricture secondary to GORD: radiography and endoscopy

Barrett’s esophagus: endoscopy and histology

Stricture

Barrett’s

Normal
Aspiration Syndromes: Chest problems

- Interstitial lung disease & pulmonary fibrosis
- Acid aspiration pneumonitis
- Aspiration pneumonia & pleural effusion
- Asthma
# GORD and Neurological conditions

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>GOR Manifestation</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral palsy or tetraplegia [1]</td>
<td>Moderately severe to severe GOR</td>
<td>10/32 (32%)</td>
</tr>
<tr>
<td>Severely Neuro-Developmentally affected [2]</td>
<td>Recurrent vomiting Confirmed GOR</td>
<td>20/136 (15%)</td>
</tr>
<tr>
<td>Vomiting patients with neuro-developmental delay and/or cerebral palsy [3]</td>
<td>Failure to thrive Respiratory symptoms Oropharyngeal incoordination</td>
<td>31/50 (62%)</td>
</tr>
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Empiric Therapy

Diagnostic Workup
Testing for GORD

- Is there a single test for GORD?
- What question does each test answer?
- How reproducible or reliable is the test?
- Does it guide our management and when is it useful?
- Does it change what we would do?
- If NOT, then…empirical therapy
Tests we can do

• Imaging
  – Barium swallow and meal
  – Video-fluoroscopy (video swallow)
  – Milk scan
• pH study
• Upper endoscopy and biopsy
• WHY NOT JUST TREAT AND MONITOR PROGRESS?
  – In any child I see, if symptoms are suggestive of reflux, I tend to avoid investigations and get on with it!
  – I save tests for the non-responders or more complicated
  – Make sure they are on enough Rx*
Goals of medical therapy

- Control symptoms
- Promote healing
- Prevent complications
- Improve health-related quality of life
- Avoid adverse effects of treatment
  - Clearly a balance to be had
What meds can we use?

• Gaviscon

• Thickeners and thickened feeds (Carobel, SMA staydown, Enfamil AR, Thick n’ easy)

• Anti-acid drugs – dose, frequency**
  – Ranitidine, **PPI** (omeprazole, lansoprazole)

• Motility agents
  – Domperidone*, metoclopramide, bethaneclid
  – Baclofen
  – Erythromycin, Ondansetron, pizotifen

• Dietary changes- Milk free, elemental etc
Approaches to Acid-Reducing Therapy

Step Down
• Begin treatment with PPI
• Maintain with PPI
• Switch to H2RA

Step Up
• Begin treatment with H2RA
• Inadequate response → PPI
• Inadequate response → ↑ PPI dose
H₂RA vs PPI in Erosive GERD

Patients healed (%)

- PPIs
- H₂RAs
- Placebo

Week 0, Week 2, Week 4, Week 6, Week 8, Week 12

H₂RA = histamine-2 receptor antagonist; PPI = proton pump inhibitor
CMPA

- CMPI and ‘allergic enteropathy’***
  - Increasingly common
  - diagnosis often NOT considered
  - NOT lactose intolerance
  - Majority better by 12 + months
  - Nb. Overlap with acid refluxers

- Treatment
  - Milk and soya free diet
  - Hypoallergenic formula
  - Nutramigen 1 and 2, Pepti Junior
  - Neocate and Neocate advance
Who is a Candidate for Antireflux Surgery in Childhood?

In my opinion, a patient who:

- Fails medical therapy due to GORD
- Is dependent on aggressive or prolonged medical therapy
- Airway safety!
  - Has persistent asthma or recurrent pneumonia due to GORD
  - Has ALTE (apnoeas, near-miss SIDS)
Principles of Antireflux Surgery

- Restore intra-abdominal segment of oesophagus
- Approximate diaphragmatic crurae
- Reduce hiatal hernia when present
- Wrap fundus around LOS to reinforce antireflux barrier
<table>
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<tr>
<th>Outcome</th>
<th>Rate (%)</th>
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<tbody>
<tr>
<td>Success rate (complete relief of symptoms)</td>
<td>57 – 92%</td>
</tr>
<tr>
<td>Mortality related to operation</td>
<td>0 – 5%</td>
</tr>
<tr>
<td>Overall complication rate</td>
<td>2 – 45%</td>
</tr>
<tr>
<td>Dumping syndrome</td>
<td>NA</td>
</tr>
<tr>
<td>Gas bloat syndrome</td>
<td>2 – 8%</td>
</tr>
<tr>
<td>Small-bowel obstruction</td>
<td>1 – 11%</td>
</tr>
<tr>
<td>Wrap failure</td>
<td>1 – 13%</td>
</tr>
<tr>
<td>Reoperation rate</td>
<td>3 – 19%</td>
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Outcomes of fundoplication: causes for concern, newer options

E Hassall

Antireflux surgery has been a mainstay of treatment for gastro-oesophageal reflux disease in children for some 40 years. In recent years, enthusiasm for antireflux surgery seems only to have increased, despite its often poor outcome, and the availability of highly effective medical therapy in the form of proton pump inhibitors (PPIs). Reports show that many children undergo surgery without reflux disease as the demonstrable cause of their symptoms/signs, and without evidence of having failed optimised medical management. Very few studies report objective testing postoperatively—those that do show high rates of failure within the first 1–3 years following surgery. Treatment with PPIs is an effective and safe alternative to surgery in many cases.

Gastro-oesophageal reflux (GOR) refers to the passage of gastric contents into the oesophagus—it is often physiological, as in many infants, and occurs postprandially in the absence of symptoms. However, abnormal reflux can lead to reflux oesophagitis, troublesome symptoms, and developmental delay. Acute gastro-oesophageal reflux can cause symptoms but, if left untreated, may lead to chronic oesophageal reflux disease (GERD) and complications. Chronic GERD may result in oesophageal strictures, Barrett’s oesophagus, and possibly adenocarcinoma. In addition, reflux can cause respiratory symptoms, such as asthma, sleep apnoea, and chronic lung disease. Severe GERD may also occur in otherwise healthy children (those without any underlying systemic disorder), especially those with a hiatal hernia, or perhaps acid hypersecretion.

Mechanisms of reflux
These are described in detail elsewhere, but explained in brief as follows. Gastrointestinal dysmotility is a major pro-reflux factor in some conditions, the term “dysmotility” referring to the absence of normal neuromuscular function of the GI tract. Normal individuals have some GO reflux, especially postprandially, but by reflex propagated peristalsis, refluxate is promptly cleared from the oesophagus back into the stomach. In the neurologically impaired (NI), the oesophagus is poorly motile, sometimes flaccid, and refluxate is not promptly cleared, leading to prolonged acid contact time and damage—that is, oesophagitis, which further impairs motor function. A prevalent mechanism of pathologic reflux is the presence of inappropriate transient lower oesophageal sphincter relaxations.
Why bother with aggressive treatment early?

• Many reasons
  – Self harm, aggressive behaviour well recognised
  – It hurts !
    • We would all want something done about it !
  – Complications must be avoided if possible
    • Distressing self harm and injury and QOL
    • Stricture
    • Barrett’s oesophagus
Conclusions

• Infant reflux usually resolves by 1-2 years

• Symptom complex and decision making

• GOR vs GORD issues:
  – physiological or pathological reflux
  – are any investigations required at all?
  – unnecessary tests for reflux frequently used
  – know limitations of diagnostic tests
  – evidence base for practice
  – NASPGHAN guideline JPGN 32; Suppl 2 2001

• Empirical therapy vs up-front testing

• Identify higher risk patients
• Are they on enough Rx?
• Liaison with surgeons
  – failed medical Rx or complications of GORD
  – medical vs surgical management (cost and efficacy)
  – 92% vs 62% ongoing use of medications
  – patient selection and pre-op evaluation is key

Spechler S, JAMA 2001
Di Lorenzo C, JPGN 2002
Constipation, gassiness, diarrhoea

- Common enough problems
- Treat aggressively, earlier!
- www.ljf.scot.nhs.uk
- Gas - air swallowing, acid related, lactose intolerance, bacterial imbalance
  - Lactose free diet
  - Antibiotics and pro-biotics
- Diarrhoea
  - Overflow with constipation ??
  - Needs properly investigated
  - Medications
Thinking outside the box!

- Association of neurological disorders with Coeliac disease
  - IBS-like symptoms
  - unexplained diarrhoea
  - weight gain problems
  - constipation
  - Particularly Down Syndrome, Turner, Williams’
  - Unexplained neurology / seizures

- Macchini, Selicorni et al, Oct 2007,

- Coeliac disease and Cornelia de Lange Syndrome: lack of association, 24 patients
Other GI Surgical issues to be aware of .....
Surgical problems- RARE, but recognised

• Diaphragmatic hernia
• Pyloric stenosis
• Annular pancreas
• Duodenal atresia
• Caecal volvulus
• Fundoplication
• Gastrostomy tube
Gastrostomy tubes / buttons
Nutrition

• Big topic!
• Dietetic input is mandatory
  – Specific growth pattern
  – See CdLS specific growth charts
  – Energy requirements must be met
  – Specific problems related to vomiting or poor absorption of calories
• SALT input – feeding clinics, MDT clinics
  – Addressed later
2-25
I'VE GOT A
SORE STOMACH.

IT DOESN'T LOOK
SORE TO ME.

YOU'LL FORGIVE ME IF I SEEK A SECOND OPINION.
Questions?

Deep Thoughts
Homer Simpson

If something's hard to do, then it's not worth doing.