GUIDELINES FOR THE MANAGEMENT OF
PAEDIATRIC GAUCHER DISEASE IN THE UNITED KINGDOM

WORKING GROUP

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INTRODUCTION

As Gaucher disease in children is rare, and the treatment may be costly, it is important that management is evaluated and reviewed. At the first National Paediatric Workshop held in London in October 1996, it was acknowledged that there were considerable differences in practice across the country, and that this was not in the best interests of the patients. It was agreed that a small working group should draw up some clinical service guidelines.

These guidelines may need to be modified in the case of certain patients with unique or difficult problems.

For purposes of this document, “children” refers to patients aged 16 and under.

Certain general rules apply:-

1. All children should be seen by paediatricians. Children should not be seen in adult centres.

2. Care should be shared with paediatricians specialising in metabolic disease, preferably at specialist centres.

There are two centres that have been designated for the diagnosis and management of paediatric Gaucher disease in the UK.

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   Contact person: Dr JE Wraith, Consultant Paediatrician

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   Contact person: Dr A Vellodi, Consultant Paediatrician
DIAGNOSIS

The definitive diagnosis of Gaucher disease must be made by enzyme assay in leukocytes or fibroblast cultures.

Chitotriosidase should be included as a screening test for all children under the age of 1 year with developmental delay and hepatosplenomegaly.

Mutational analysis should be routinely carried out.

All siblings, and both parents, of the propositus should be routinely tested.
INITIAL ASSESSMENT

This should consist of the following:-

1. History.
2. Clinical examination.
3. Laboratory tests.
4. Imaging.
5. Other tests.

1. HISTORY

Specific note should be made of the following:-

1. Failure to thrive/poor growth.
2. “Not being quite right”.
3. Pallor.
4. Abdominal distention.
5. Bruising.
7. Fractures.
11. Splenectomy - whether partial or complete.
12. Need for transfusions.
13. Shortness of breath.
2. **CLINICAL EXAMINATION**

A routine clinical examination should be performed. Particular note should be made of the following:

1. Height, weight and head circumference.
2. Pubertal status.
3. Pallor.
4. Icterus.
5. Ecchymoses, petechiae.
7. Spinal deformity.
8. Any evidence of respiratory distress.
9. Neurological signs, including gaze palsy.
10. Cardiac assessment including echocardiography.
11. Neuropsychometry.
12. Peak expiratory flow rate (PEFR) if compliant.

3. **LABORATORY INVESTIGATIONS**

   **A. Haematology**

1. Full blood count, retic count.
2. Coagulation screen (PT, APTT, TT).
3. Clotting factor levels if indicated by the coagulation screen.
4. Serum iron, TIBC if Hb is low.

   **B. Biochemistry**

1. Urea and electrolytes.
2. Liver function tests.
3. Angiotensin-converting enzyme.
C. Immunology

1. Encapsulated organism antibodies (pneumococcal, HIB, meningococcal).

2. *Cerezyme antibody levels. Antibody status is no longer required for patients treated with Ceredase, unless at the request of the managing clinician.

*Antibody status for Cerezyme treated patients is required at the following intervals:-
Baseline before treatment starts and every three months for the first year. Subsequently, twice yearly for the second year, and once yearly thereafter.

D. Molecular Genetics

DNA analysis for common mutations (including sequencing exons 9-10).

E. Histology

Baseline liver biopsy in selected patients (advice to be sought from paediatric referral centre.

4. IMAGING

A. Plain Radiography

1. Skeletal survey (to include chest, proximal humeri/shoulder joints, AP pelvis/proximal femurs, both knees AP and whole spine AP/lat)
2. Bone age.

B. MRI

1. Sagittal T1 spine.
2. Coronal T1 and coronal STIR of lower pelvis and femora.
3. Coronal T1 abdomen.
C. Ultrasound

1. Measure liver length and take longitudinal image of aorta.
2. Three dimensions of the spleen; length to be compared to normal values.
3. Doppler examination of the portal vein, to demonstrate portal vein flow, and assessment of presence or absence of varices.

5. OTHER TESTS

1. Eye movements.
2. Echocardiogram.
3. Lung function if compliant (including TCO).
4. Auditory evoked potentials (BSAEP).)
5. EEG. ) Type III only
6. Neuropsychometry  )
# FOLLOW-UP ASSESSMENTS

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<tr>
<th></th>
<th>Frequency (months)</th>
<th>Whether IP or OP</th>
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<tr>
<td>Ht &amp; Wt</td>
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<td>OP</td>
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<td>3</td>
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<tr>
<td>Spleen</td>
<td>3</td>
<td>OP</td>
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<tr>
<td>Neuropsych</td>
<td>12</td>
<td>OP/OP</td>
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| **LABORATORY**       |                   |                 |
| HAEMATOLOGY          |                   |                 |
| FBC, retics         | 3 till normal then 12 | OP/IP         |
| Clotting            | 12 or pre-op      | OP/IP           |

| **BIOCHEMISTRY**     |                   |                 |
| ACE                  | 3                 | OP/IP           |
| Total AP             | 3                 | OP/IP           |
| Chitotriosidase      | 3                 | OP/IP           |

| **IMMUNOLOGY**       |                   |                 |
| Cerezyme antibodies  | * See text        | OP/IP           |
**IMAGING**

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<thead>
<tr>
<th>Test</th>
<th>Frequency</th>
<th>Site</th>
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<tbody>
<tr>
<td>Limited skeletal survey (chest, proximal humeri/shoulder joints, AP pelvis/proximal femurs, both knees AP)</td>
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<td>OP</td>
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<tr>
<td>MRI as in initial MRI</td>
<td>As needed</td>
<td>IP/OP</td>
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<tr>
<td>USS &amp; Doppler</td>
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<td>IP/OP</td>
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**OTHER TESTS**

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<thead>
<tr>
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<th>Frequency</th>
<th>Site</th>
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<tbody>
<tr>
<td>Eye movements (Type III only)</td>
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<td>IP/OP</td>
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<tr>
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<td>12</td>
<td>IP</td>
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### FOLLOW-UP PLAN

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<td>Total AP</td>
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<td>+</td>
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<tr>
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<td><strong>IMAGING</strong></td>
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<tr>
<td>X-rays hip &amp; spine</td>
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TREATMENT WITH ENZYME REPLACEMENT THERAPY (ERT)

All children with type 1 Gaucher disease should commence treatment with enzyme replacement therapy.

All decisions regarding dose amendments should be made in consultation with a specialist unit.

Enzyme replacement therapy is not recommended for children with Type II disease.

**Type 1 Disease**

For children with Type 1 disease, the recommended starting dose is 60U/kg every 2 weeks by intravenous infusion.

Monitoring should be performed as described above.

The dose should be frequently reviewed and increased according to weight gain.

There should be no reduction in dose for the first six months. Subsequent dose reduction should take into account the following:-

- a) clinical response (including growth)
- b) haematological and biochemical response
- c) Changes seen on imaging (visceral and skeletal responses)

The dose may be reduced provided that

- a) Clinical response is satisfactory, and
- b) Haematological parameters (full blood count) are normal
- c) Biochemical parameters are improving, with satisfactory falls in acid phosphatase, angiotensin converting enzyme and plasma chitotriosidase levels.

The dose should be reviewed every six months. Reduction should not take place more frequently than this.

The minimum dose should not be less than 30 units/kg every 2 weeks.
**Type III Disease**

For children with Type III, the starting dose should be 120 units/kg every 2 weeks.

If there is any evidence of neurological deterioration, consideration may be given to bone marrow transplantation.

Skeletal disease which appears to be non-responsive or progressing despite adequate dosing will need to be evaluated in more detail. Bisphosphonates may have a role to play in the management of skeletal involvement. Their use should be initiated at, and supervised by, a specialist unit.

The management of neuronopathic disease has been the subject of a detailed analysis by a European Task Force, and a consensus report has been published. On the whole, both centres have agreed to follow these guidelines. However, as a result of an audiology audit carried out in June 2001, it has been decided that BAER will be used only as part of the initial assessment and not for routine follow up.