European Porphyria Network: providing better healthcare for patients and their families

Pilot European Reference Network from 2007-2010
Operating grants in 2011 & 2012

Samantha Parker on behalf of Professor Jean-Charles Deybach
Porphyrias

“Obscure diseases with confusing names considered only when the need for a diagnosis is desperate”

- ALAD Deficiency Porphyria
- Acute Intermittent Porphyria
- Hereditary Coproporphyria
- Variegate Porphyria
- Porphyria Cutanea tarda
- Congenital Erythropoïetic Porphyria
- Erythropoïetic Protoporphyria
- X Linked Dominant Protoporphyria

red urines
Porphyrias

...from greek « porphyros » : red pigment

- 8 rare genetic diseases (*prevalence ~1/100 000 ?*)
- Due to a partial deficiency in one of the enzymes of the heme biosynthetic pathway
- Each related to specific mutations in their encoding genes
- Abnormal accumulation and excretion of porphyrins and their precursors urine, feces, blood)
- Intermittent acute neuro-visceral attacks and/or specific photo-induced skin lesions
Porphyrias

puzzling features

• Mostly dominant in inheritance
• Acute symptoms precipitated by endo / exogenous factors: hormones, infections, stress, drugs ... pharmacogenetic diseases
• Pathophysiology largely unknown:
  • Large allelic heterogeneity
  • No genotype-phenotype relationship
  • No animal model

...why patients are patients?
Why a European Porphyria Network?

- Most healthcare professionals have no experience diagnosing and treating porphyria patients
- Disparity in the content and accessibility of information
- Conflicting data on safety of drugs in acute porphyrias
- Epidemiology unknown: incidence, prevalence, types of complications...
- Limited number of patients, limited research resources... in each EU country
- Existing Porphyria Centers of Expertise in some EU countries >> Centre Français des Porphyries as Coordinating Center of EPNET
Partners 2012 (National Centres of Expertise or recognised with expertise)

Network of expert centres expanded from 20 members in 14 countries to 33 members in 21 countries (2012)
Partners 2012 (Across the globe)
Membership criteria

1. Able to distinguish, using biochemical testing, between all types of porphyria
2. Able to offer specialist detailed interpretation of results with clinical advice on management
3. Participate EPNET organised quality assurance schemes (now self-funding)
General objectives

1. Have a registered specialist centre in every EU country
2. Improve diagnostic and analytical quality of specialist porphyria centres in Europe and reduce delay to diagnosis
3. Collect long term follow-up into the European porphyria registry
4. Best practice guidelines
5. Disseminate information about drugs
6. Promote and facilitate research
Patient consensus-agreed Information

1. Patient information leaflets for all porphyrias in European languages
2. Improved detailed consensus agreed information for health care professionals
3. www.porphyria-europe.org
Porphyria Registry

- Incidence data for 5 inherited porphyrias
  - AIP, VP, HCP, CEP and EPP
- Prevalence/incidence of rare complications in acute porphyrias
- Clinical details of acute porphyrias
## Incidence of inherited porphyrias
(new symptomatic cases/year/million)

<table>
<thead>
<tr>
<th>Country</th>
<th>Population (millions)</th>
<th>AIP</th>
<th>HCP</th>
<th>VP</th>
<th>EPP</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>64.71</td>
<td>0.11</td>
<td>0.01</td>
<td>0.12</td>
<td>0.06</td>
</tr>
<tr>
<td>Ireland</td>
<td>4.45</td>
<td>0</td>
<td>0</td>
<td>0.16</td>
<td>0.08</td>
</tr>
<tr>
<td>N. Italy</td>
<td>27</td>
<td>0.11</td>
<td>0.03</td>
<td>0.05</td>
<td>0.06</td>
</tr>
<tr>
<td>Italy</td>
<td>60.4</td>
<td>-</td>
<td>-</td>
<td>0.06</td>
<td>0.07</td>
</tr>
<tr>
<td>Netherlands</td>
<td>16.58</td>
<td>0.18</td>
<td>0.02</td>
<td>0.06</td>
<td>0.18</td>
</tr>
<tr>
<td>Norway</td>
<td>4.85</td>
<td>0.14</td>
<td>0</td>
<td>0.07</td>
<td>0.36</td>
</tr>
<tr>
<td>Poland</td>
<td>38.16</td>
<td>0.16</td>
<td>0</td>
<td>0.01</td>
<td>0.02</td>
</tr>
<tr>
<td>Spain</td>
<td>46.09</td>
<td>0.12</td>
<td>0.04</td>
<td>0.04</td>
<td>0.03</td>
</tr>
<tr>
<td>Sweden</td>
<td>9.35</td>
<td>0.51</td>
<td>0</td>
<td>0.11</td>
<td>0.18</td>
</tr>
<tr>
<td>Switzerland</td>
<td>7.76</td>
<td>0.35</td>
<td>0.04</td>
<td>0.26</td>
<td>0.35</td>
</tr>
<tr>
<td>UK</td>
<td>62.04</td>
<td>0.16</td>
<td>0.04</td>
<td>0.08</td>
<td>0.33</td>
</tr>
<tr>
<td>All countries</td>
<td>314.39</td>
<td>0.13*</td>
<td>0.02</td>
<td>0.08</td>
<td>0.12</td>
</tr>
</tbody>
</table>
Complications (Acute Porphyrias)

- Recurrent acute attacks
  - 67 patients (64 AIP; 3 VP)
  - AIP: 53 females; median age 36 (23-68) years
  - 11 males; median age 43.5 (17-52) years
- Liver transplant for AIP; 13 patients
- Estimated percentages of new symptomatic patients who will develop recurrent acute attacks:
  - Females: 8.2 %
  - Males: 5.6 %
Primary liver cancer (HCC) in Acute Intermittent Porphyria

- Prospective survey over 3 year period
- 12 new cases: 9 females, 3 males; age: 60 – 81 years

<table>
<thead>
<tr>
<th>Country</th>
<th>New cases Per 3 years</th>
<th>Population (million)</th>
<th>Incidence AIP</th>
<th>Incidence HCC in AIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweden</td>
<td>9* (7 AIP, 2 VP)</td>
<td>9.35</td>
<td>0.51 (x 4)</td>
<td>0.25 (x 63)</td>
</tr>
<tr>
<td>CH, F, NL, UK</td>
<td>3 (2 AIP, 1 VP)</td>
<td>151.09</td>
<td>0.13</td>
<td>0.004</td>
</tr>
</tbody>
</table>
Porphyria European Quality Assay scheme

**u-ALA [µmol/mmol creatinine] reported by 28 out of 28 laboratories**

### Historical data:

<table>
<thead>
<tr>
<th>Survey</th>
<th>Median</th>
<th>Your value</th>
<th>Dev. %</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/10</td>
<td>3.8</td>
<td>4.0</td>
<td>5.3</td>
</tr>
<tr>
<td>1/10</td>
<td>7.7</td>
<td>7.7</td>
<td>0.0</td>
</tr>
<tr>
<td>2/09</td>
<td>7.6</td>
<td>7.2</td>
<td>-5.4</td>
</tr>
<tr>
<td>1/09</td>
<td>2.1</td>
<td>2.3</td>
<td>9.5</td>
</tr>
<tr>
<td>2/08</td>
<td>1.7</td>
<td>1.8</td>
<td>5.9</td>
</tr>
<tr>
<td>1/08</td>
<td>63.8</td>
<td>63.2</td>
<td>-0.9</td>
</tr>
</tbody>
</table>

### Deviation (%) vs Deviation (concentration)

Self funding through subscription
Publications

1. Peer reviewed publication on external quality assessment
2. Peer reviewed publication on porphyria related laboratory and clinical activity presenting nominative data
3. Peer reviewed publication presenting an evidence based diagnostic strategy for the porphyrias
4. Peer reviewed publication describing the methods for collecting clinical data and resulting impact on drug safety assessments
5. Paper on the incidence and long-term complications
Conclusions

- EPNET is now a well established European Reference Network on a group of Rare Diseases.
- EPNET Member’s continuing enthusiasm and momentum are key factors in demonstrating the network’s sustainability.
- Great effort has been spent in efficiently running, coordinating, expanding the network and establishing the European Porphyria Registry;
- These are powerful reasons for continuing.
ACKNOWLEDGEMENTS

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