Open collaboration for research

8 steps from Black Bone Disease

Dr Nicolas Sireau
Chairman and CEO, AKU Society
Chairman and Co-founder, Findacure
1902: Sir Archibald Garrod
THE LANCET, JULY 11, 1908.

The Croonian Lectures on
INBORN ERRORS OF METABOLISM.
Delivered before the Royal College of Physicians of London on June 18th, 23rd, 25th, and 30th, 1908,

BY ARCHIBALD E. GARROD, M.A., M.D.
OXON., F.R.C.P. LOND.,
ASSISTANT PHYSICIAN TO, AND LECTURER ON CHEMICAL PATHOLOGY AT, ST. BARTHOLOMEW'S HOSPITAL; SENIOR PHYSICIAN, HOSPITAL FOR SICK CHILDREN, GREAT ORMOND STREET.

LECTURE II.¹
Delivered on June 23rd.

ALKAPTONURIA.

MR. PRESIDENT AND FELLOWS.—Of inborn errors of metabolism, alkaptonuria is that of which we know most, and from the study of which most has been learnt. In itself it is a trifling matter, inconvenient rather than harmful, which only attracts attention because an infant stains its clothing, or because an adult fails to effect an insurance of his life. The medical man merely needs to be aware of its existence and to be acquainted with the methods for its recognition in order that he may not mistake it for troubles of graver kinds; but for the chemical physiologist and pathologist it is one of the most interesting of metabolic

the early years of the nineteen
twenty-black when passed and such as but it is difficult to suggest an
alkaptonuria for some cases
sixteenth and seventeenth century
G. A. Scribonius⁴ (in 1584) of
enjoyed good health, continuous
cited by Schenck⁶ (in 1602)
similar peculiarity and stated
life. The most interesting reco
in the work of Zacutus Lusitan
patient was a boy who passed
age of 14 years, was submit
tment which had for its aim the
his viscera, which was supposed
in question by charring and
the measures prescribed were
cold and watery diet, and drug
any obvious effect, and eventual
the futile and superfluous ther
their natural course. None of
married, begat a large family,
life, always passing urine black

That alkaptonuria is a very
question, and many medical na
ever met with it. Of its occu
a family and of its mode
spoken at sufficient length in
majority of instances it is pre
throughout life, but has been su
Harwa

Oldest AKU Patient
1500 BC

Stenn et al 1977
Step 1:

Working with scientists to understand the disease
Metabolic pathway

- **Alkaptonuria**
  - Phenylalanine
  - 4-hydroxy-phenylpyruvic acid dioxygenase

- **Phenylketonuria**
  - Tyrosine → DOPA → Melanin
  - Nitisinone

- **Albinism**
  - Tyrosine

- **Alkaptonuria**
  - Maleylacetoacetate
  - Fumarylacetoacetate
  - Succinylacetone

- **Tyrosinaemia type 1**
  - Phenylalanine hydroxylase
The AKU tetrad
Effects on spine

Sofia Michopoulou & Andrew Todd Pokropek
A cell model

AKU Research Team
AKU mouse model
Nitisinone
Nitisinone reduces homogentisic acid by 95%
Urinary HGA

Figure 1.

National Institutes of Health
Urinary HGA
Step 2:

Working with clinicians for a centre of excellence
The Robert Gregory National Alkaptonuria Centre

Funded by NHS England
Step 3:

Working with clinical trial centres
## Three Studies

<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Description</th>
<th>Sites</th>
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<tr>
<td><strong>SONIA 1</strong>: Suitability of Nitisinone in Alkaptonuria 1</td>
<td>3-month phase II study</td>
<td>UK/Slovakia</td>
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<tr>
<td><strong>SONIA 2</strong>: Suitability of Nitisinone in Alkaptonuria 2</td>
<td>4-year phase III</td>
<td>UK/Slovakia/France</td>
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<tr>
<td><strong>SOFIA</strong>: Subclinical Ochronosis Features in Alkaptonuria</td>
<td>Cross-sectional study</td>
<td>UK</td>
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Three Clinical Trial Sites

1) Liverpool, UK
   Royal Liverpool University Hospital
   PI: Prof L Ranganath

2) Paris, France
   Hôpital Necker
   PI: Prof Pascale de Lonlay

3) Piešťany, Slovakia
   National Institute of Rheumatic Disease
   PI: Prof Jozef Rovenský
Step 4:
Working as a consortium with industry
The DevelopAKUre partners

The Royal Liverpool and Broadgreen University Hospitals

University of Liverpool

Hôpital Necker Enfants Malades

PSR the orphan EXPERTS

UDOS Drug development consultancy

Institut Necker

University of Siena

Sobi SWEDISH ORPHAN BIOVITRUM

nordic bioscience

AKU Alkaptonuria Society

ALCAP Association pour la Lutte Contre l’Alcaptonurie
Step 5:

Working with patients around the world
A global patient movement

Worldwide: 950 patients and counting
Social media

- Facebook
- Twitter
- Google +
- Pinterest
Curing Black Bone Disease

More than 110 years since its discovery, we're trialling the world's first treatment for AKU. Find out more.

AKU News
National Coverage for Bones and Joints
Musculoskeletal conditions (MSKs) are the greatest cause of disability... more...

Twitter
AKU Society @findAKU
This week's blog post: National Coverage for bonesandjoints conditions such as Black Bone Disease: bit.ly/Je2iMf @MediaplanetUK

AKU Events
Announcing Our Second Patient Workshop: 17th October
Meet others with AKU, while hearing presentations about pain management... more...
AKU Societies in EU, Asia, Middle East and North America

- AKU Society UK
- ALCAP (France)
- AIMAKU (Italy)
- AKU Society Germany
- AKU Society Netherlands
- AKU Society Jordan
- AKU Society India
- AKU Society Slovakia
- AKU Society North America (USA and Canada)
- AKU Society Belgium (in progress)
- AKU Society Sweden (in progress)
- AKU Society Asia (in progress)
HELP US CURE BLACK BONE DISEASE
Cure Black Bone Disease

Three years ago, Nick gave up his job to devote himself to find a cure for Black Bone Disease, which affects his boys. Please help him by donating now!

Health – Cambridge, United Kingdom

$98,685

Raised of $98,000 Goal

0 time left

Flexible Funding
This campaign has ended and will receive all funds raised. Funding duration: August 31, 2013 - October 20, 2013 (11:59pm PT).

Select a Perk for your contribution

$11
Your name on our website!

For an $11 donation, you will get your name on the website.
AKU patient Ann

HELP US CURE BLACK BONE DISEASE
Prof Ranganath, Coordinator of DevelopAKUre

HELP US CURE BLACK BONE DISEASE
We made it!

Our campaign had 28,598 visits over 50 days which led to 1469 donors from 40 countries donating a total of $98,685 on Indiegogo. $22,327 was also donated offline taking us to a grand total of $121,012.

We couldn’t have done it without your help. Every dollar donated and every email, tweet or Facebook post sent has helped us reach our goal. So we would like to say a great big THANK YOU.
"These trials have given us great hope. This treatment could completely change our lives. We’re that one step closer to a cure.”

- Belgium AKU patient
AKU patients
Brenda, Sharon and Jennifer
Step 6: Learning from other patient groups
The Voice of Rare Disease Patients in Europe

Involving patients in developing rare disease guidelines

EU Clinical Trials Register
RARE-Bestpractices
International Rare Diseases Research Consortium
EURORDIS Summer School

Patients and services
- Elysha didn’t sit around being sick at Barretstown Therapeutic Recreation Programme. She had nonstop fun!

Featured Event
- Don’t miss the chance to download the speaker presentations, available online and on the mobile app

Members’ Corner
- Findacure Training workshop: How to develop clinical trials as a small patient group. 24 July, London, UK

EURORDIS TV
- Watch EURORDIS TV's video of the week!

EURORDIS is a non-governmental patient-driven alliance of patient organisations representing 634 rare disease patient organisations in 68 countries covering over 4000 diseases.
Step 7:
Working more broadly with other stakeholders
Step 8:
Sharing with the wider stakeholder community
Rare Diseases: Challenges and Opportunities for Social Entrepreneurs

Out now!

With chapters from leaders in the rare disease sector

Contact: nick@akusociety.org