Genetic Services and What’s Happening in the Real World

➢ Good clinical services: Codified consultations
➢ Sound genetic diagnostic testing

**Prosper Lukusa, MD, PhD**  
Centre for Human Genetics, University of Kinshasa, DR Congo  
Congolese Society for Human Genetics, CoSHG  
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Basic structure of a standard modern genetic service

➢ Modern hospitals

➢ Modern infrastructure

➢ Highly equipped labo

Highly trained - Physicians

Financial support available

➢ Medical insurance

Accessibility of clinical services for each patient

Service providers

ELSI

➢ Laboratory staff
What is the situation in the real world, as in my country, the DRC?

- No modernization of Hospitals
- Electricity / Water supply??
- Heavy socio-economical difficulties
- Equipment
- Supplies
- Lack of well trained geneticist: DRC -> 3 for 80,000,000 inhabitants
- Erroneous cultural & traditional believes = Heavy barrier

Low development, no official local funding
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Service providers

Aim: to turn each challenge into Opportunity to do something

- Patients → limited income

Strategies

→ How to face?

Aim: to turn each challenge into Opportunity to do something
Strategy 1: Initiate and obtain funded research projects allowing to reach specific objectives:

- To train adequately local geneticists
- To obtain basic laboratory equipment
- To run good and updated clinical services
- To offer either free or not too expensive services
- To reach adequate population education: Conferences & workshops; network of patient associations: SCA, DD, Albinism
Examples of funded research projects we initiated

➢ 2007-2012: “Initiation to genetics practice” (IOM): training of physicians + Conferences to break mystical believes

➢ 2010-2015: “Clinical and genetic study of intellectual disability in DRC” (IRO)

➢ 2015-2018: “Implementation of simple and affordable molecular testing for sickle cell anemia and effect of hydroxyurea treatment on clinical and biochemical evolution in DR Congo” (VLIER-UOS)

➢ 2015-2018: “Genetics of albinism in DRC” (Genetics Chair for Congo)

➔ As indirect benefits: geneticists training, basic equipment, affordable clinical services, population education
Strategy 2: Share existing resources with other laboratories

• From Europe: North (high quality testing)–South (protocol) partnership
  Example: - North: Deciphering Developmental Delay consortium (UK)
  - South: DDD – Africa consortium (South Africa & DRC)
  ➔ This partnership enables us to leverage WES and bioinformatics expertise existing in UK (at the Wellcome Trust Sanger Institute)

• From Africa: South – South partnerships with specific tasks
  Example: - South-Africa (National Health Lab Service)
  - DRC (Center for Human Genetics, University of Kinshasa)
  ➔ MLPA analysis in SA (for copy number variations studies)
Strategy 3: Adopt methods allowing to skirt lack of regular electricity or water

• Implement simple testing methods: sample collection on dry spots, testing without prior DNA extraction

• Purchase of lyophilized reagents (less restricting)
Strategy 4: Combine Intra and extramural consultations

Often, lack of money (for transportation and consultation) → patient from coming to doctor
Sickle Cell Anemia:
Minimal laboratory equipment for investigations: Strategy?

Project ("TEAM PROJECT"):
“IMPLEMENTATION OF SIMPLE AND AFFORDABLE MOLECULAR TESTING FOR SICKLE CELL ANEMIA DIAGNOSIS AND CONTROLLED TREATMENT BY HYDROXYUREA IN DR CONGO”.

➔ VLIR-UOS (Belgium) FUNDING
SCA = real public health problem

- DRC = 3rd most affected country worldwide (after India, Nigeria)
  - 40,000 newborns/Y (OMS, 2011)
  - 16.9 – 33% AS (Bitue et al, 2017)
  - 1.4-3% SS (Tshilolo et al, 2009; Pan Afr Med J, 2014)
  - High death rates of SCA patients
    - 50% ≤ 2 years age (ACP, 2017)
    - 75% ≤ 5 years age (PNLCD, 2017)

⇒ Real big challenges
Main Challenges

➢ Huge needs:
   - Too large country: 2 344 858 km²
   - Too populated, with 1/4-1/3 Carriers

➢ No tradition of Prenuptial screening

➢ Mystical believes (low literacy)

➢ High incidence of poverty: 71.34 %;
   ➔ >70% patients from very poor families
   (59% population live with < 1 USD/day!)

➢ Large families: Fertility rate: 5.91 – 6.45 children/woman)

➢ High cost of analyses: ± 30 USD/ Electrophoresis in private labo

➢ No official funding, no medical insurance

➔ Every step should be initiated by us
TEAM PROJECT ON SICKLE CELL ANEMIA (VLIR/UOS)

Official objective: Improve diagnosis and treatment of SCA in DRC:

➢ Conduct awareness campaign about SCD

➢ Conduct trial with HU to assess its clinical & biological efficacy in DRC patients

➢ Confirm SCA diagnosis by biochemical & molecular analysis
  - SCA diagnosis often not confirmed prior to transfusions (made in peripheral health centers or in dispensaries)
  - Some false positive/negative results after acetate cellulose electrophoresis (commonly used diagnostic test).

➔ Capillary electrophoresis & Cheep procedure for molecular test
TEAM PROJECT ON SICKLE CELL ANEMIA (VLIR/UOS)

Indirect benefits:

➢ 3 bursal PhD students working on diagnosis procedures (1), on clinical evolution of children (2) & adults (3) under hydrea.

➢ Interesting equipment for the laboratory:
  - Minicap for Hb electrophoresis
  - Thermocyclers for PCR
  - Transilluminator

➢ Hydrea for free treatment of 300 patients during 2 years

➢ Laptop, slide projector and funding for awareness campaign (conferences & workshops to break mystical, false believes)
Provisional results: encouraging

• Compared EDTA tubes, FTA cards were demonstrated to be a cheaper (5$ -> 15$) and better alternative method for DNA extraction and storage in our limited resources setting.

• Molecular testing (DdeI restriction enzyme $\rightarrow$ E6V mutat.) revealed 19/141 patients (>13%) who had been wrongly classified as SCD patients on basis of classical electrophoresis.

• First year biological (HbF, Hb, WBC, LDH...) and clinical (crises, transfusions...) evaluations of the patients under HU trial show improving evolution.
General Conclusion

• It is true that implementing and running genetic service in the “real world” is more difficult than “in theory”.

• But, each difficulty offers unique opportunities for scientific researchers and also for the community to make a step forward.

• A helping hand from genetic companies or private funding agencies, and a stronger South-South partnership can make things much easier.
Thank you for your attention
Perspectives

• The clinical presentation of SCD appeared to be influenced in DRC too by HbF levels and coinheritance with α-thalassemia: 49% of adult patients in each class (Mikobi et al., 2017; 2018).

• Molecular research on some polymorphisms (BCL11A and HMIP SNP’s) and their correlation with HPFH among Congolese SCA patients (that could influence disease severity and response to HU treatment) is still ongoing, in partnership with the KU Leuven laboratory of Human Genetics.