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Ethics and Vulnerable Population

- The patients with Rare Diseases are a particularly vulnerable population in all parts of the world, but especially in developing countries where patients are very susceptible to be harmed by action or omission.

Items to be discussed

- Diagnosis.
  - Prenatal
  - Newborn.
  - Adult
  - Pre-implantation
- Research
  - Children
  - Communities.
  - Informed consent.
- Orphan Drugs
- Biobanks

Problems that affect patients and their families

- Only close to 80% of RD are of genetic origin, the others maybe transmissible or have different etiology . However some common features of RD are:
- Delay in the diagnosis produces:

1. Helplessness and hopeless sensation in the family.

- Feeling of abandonment by the Health System.
- Sense of guilt towards oneself and his or her partner.
- Social exclusion .
- Economical problems due to the high costs of treatment or inability to work because one member of the couple has to take care of the patient. .Family collapse and dissolution.
- Use of ineffective or harmful alternative medicines.

Neonatal Diagnosis

- When should be done?

- "If the prevalence of the disease is relatively common, within the rare diseases.
- Reliable diagnostic methods should be available.
- Availability of effective treatment
- Cost/Benefit economically favorable .
- It should not exclude
- Only should be done if there is follow-up and treatment guaranteed for the patient.

Molecular Diagnosis

- It is feasible in a single cell. Before birth, and many years after death.
- Treatment availability limited but is increasing very fast even in developing countries.
- Could be done long before the symptoms appear in late onset diseases such as:
  - Metachromatic Leucodystrophy
  - Huntington's Chorea
  - Tay Sachs Disease.

Prenatal Diagnosis

- May be used in:

- Diseases for which there is no treatment such as catastrophic neurodegenerative diseases.
  - It is generally required when the family is willing to interrupt the pregnancy usually in very severe cases). Interruption of pregnancy is banned in many countries. In others it is legally permitted for some diseases with very bad neonatal outcome.
- In diseases in which it is possible to prevent symptoms since birth.

Prenatal Diagnosis

- May be done in one single cell. During early phases of pregnancy. Before implantation in case of in vitro fertilization.
- Is there any treatment? If no treatment available can its severity and prognosis be predicted?
- Is it a devastating disease?
- What will be the age of onset, for example Huntigton's chorea.

Prenatal diagnosis

- Diseases in which the symptoms can be prevented.
- Neurodegenerative catastrophic diseases.
- Diseases with no treatment available.
- Pregnancy interruption possibility.

Newborn Screening

- When should it be performed?
  - High incidence.
  - Treatment availability.
  - Cost-effectiveness.
  - Can complications be prevented? Is it not costly?
  - It can be performed up to 40 diseases. It may be done if treatment and follow-up are guaranteed.

Pre-implantatory Diagnosis

- Possible In selected diseases . Opposition due to religous beliefs. Not should be used to select the sex of the child.

Adult Onset Diseases

- Possible for many genetic diseases and it is very convenient if there is treatment available or onset is triggered by drugs or special circumstances that may be avoided.
- Is there treatment available?
- If no treatment, would the patient still want to be diagnosed?
- Will the patient sue the physician if no diagnosis assay is ordered?

Reasons to promote participation in research projects

- Low number of patient's globally, therefore is necessary to include patients from many countries as possible.
- Efficacy or adverse effects for some medications are associated with genetic characteristics that must be studied for each population.
- For some developing countries families must pressure the health system to obtain care and inclusion in clinical studies.

Research in children

- Children must be treated as such. They are not "small adults".
- Most research studies are conducted in adults and frequently are extrapolated to children without proper adjustments.
- Medications have risks and special indications in children.
- Therefore it is necessary to do well designed and properly controlled clinical assays in children..

Research

- The sequencing of the human genome provides new knowledge opportunities for science. It should be emphasized that research must respect human dignity, decision freedom and human rights, avoiding any kind of discrimination based on genetic characteristics. *Unesco. (2008). Declaración Universal sobre Bioética y Derechos Humanos.*

In Native Communities.

- Personal Beliefs must be respected.
- Biological samples can only be used for purposes authorized by the patient.
- It must be specified that the samples are to be destroyed after assays.
- Safety issues must be taken into account to protect not only the patients but the researchers and the enviroment.

Guidelines for subjects participating in research projetcts.

- Informed consent must be obtained.
- Consent must describe objectives and research details, benefits for either patient or research, risks and alternatives. It must state that the patient can quit the study at any time, without penalty.
- Patient's autonomy must be taken into account. In the case of children their right to not participate must be respected.

Ethics committee.

- The ethics committees must study not only the ethical aspects of the projects, but also the relevance from the scientific point of view, safety and the design. If conditions such as sample size and pertinence are not met by the project, it should not be approved.
- The committees should follow-up the development of the projects, and should recommend appropriate actions in case the study have to be suspended or patients have to be withdrawn.
- A member of the community must participate in the committee.
- The committee must insist on the application of national and international guidelines.

Orphan drugs

- Cost must be proportional to the investment. Profit must be stimulating for industry, but there should not be speculation with the prices.
- There is no justification for the indecent higher prizes of orphan drugs in some developing countries compared with developed countries.
- Why that situation has been tolerated? Because of negligence, poor negotiations, corruption? Why is service managed by the private sector with profit rather than service interests.

Biobanks

- Samples can be stored for future use for research and development of new medications and procedures. When an open authorization to use samples in future research is justified and permissible? If the patient authorizes that his or her samples be used for those purposes it must be foreseen what benefits the donor will receive if a marketable product is developed.

Informed consent

- Terms and conditions
  - The person signing should understand all terms and conditions.
  - Tribe chief or legal guardian should be informed.
  - Who should sign. Parents or legal guardian. In some cases subjects older than 12years old are considered competent to sign. It is excluded persons if not in full use of their mental faculties.
  - Participation must be free and spontaneous and not influenced by economical reasons or to meet the treating physician's desires.
  - There shuld be no inadequate pressures. Participants from all countries should benefit equally.

Informed consent

- There should be no pressures.
- Subject must approved either by signature or fingerprint or trough legal guardian.
- Researcher must assure that the patient fully understands the information included in the consent specially the risks, benefits, alternatives and withdrawal.

Research in Children

- Can be compensated, but should not comply with particular interests.
- Who should authorize the consent?
- When can it not be carried out in adults?
- When is it permitted?
- Patient should not be put at risk.

Orphan drugs

- Not all are high-cost. There are medium and low-cost. The paradox is that the cheaper the dug is the more orphan it becomes.
- New therapies: enzyme replacement, gene therapy, stem cells and chaperones.
- For most of them there is no treatment available. However it is our duty to provide the best quality of life for the patients and his or her families. Genetic, family and psychological counseling should be offered.

Research

- Informed signed consent
- Terms and conditions
  - The person signining should understand all terms and conditions.
  - Tribe chief or legal guardian.
  - Who should sign. Subject older tah 14 years old.
  - Legal guardian.
  - Free and spontaneous.