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6th Genodermatoses in Mediterranean working session
1st TAG meeting

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Genodermatoses in the Palestinian Territories

Preliminary Report

Introduction

- Since June 1967,the West Bank of Jordan and the Gaza Strip are under the Israeli Occupation which kept our medical services undeveloped and annexed.

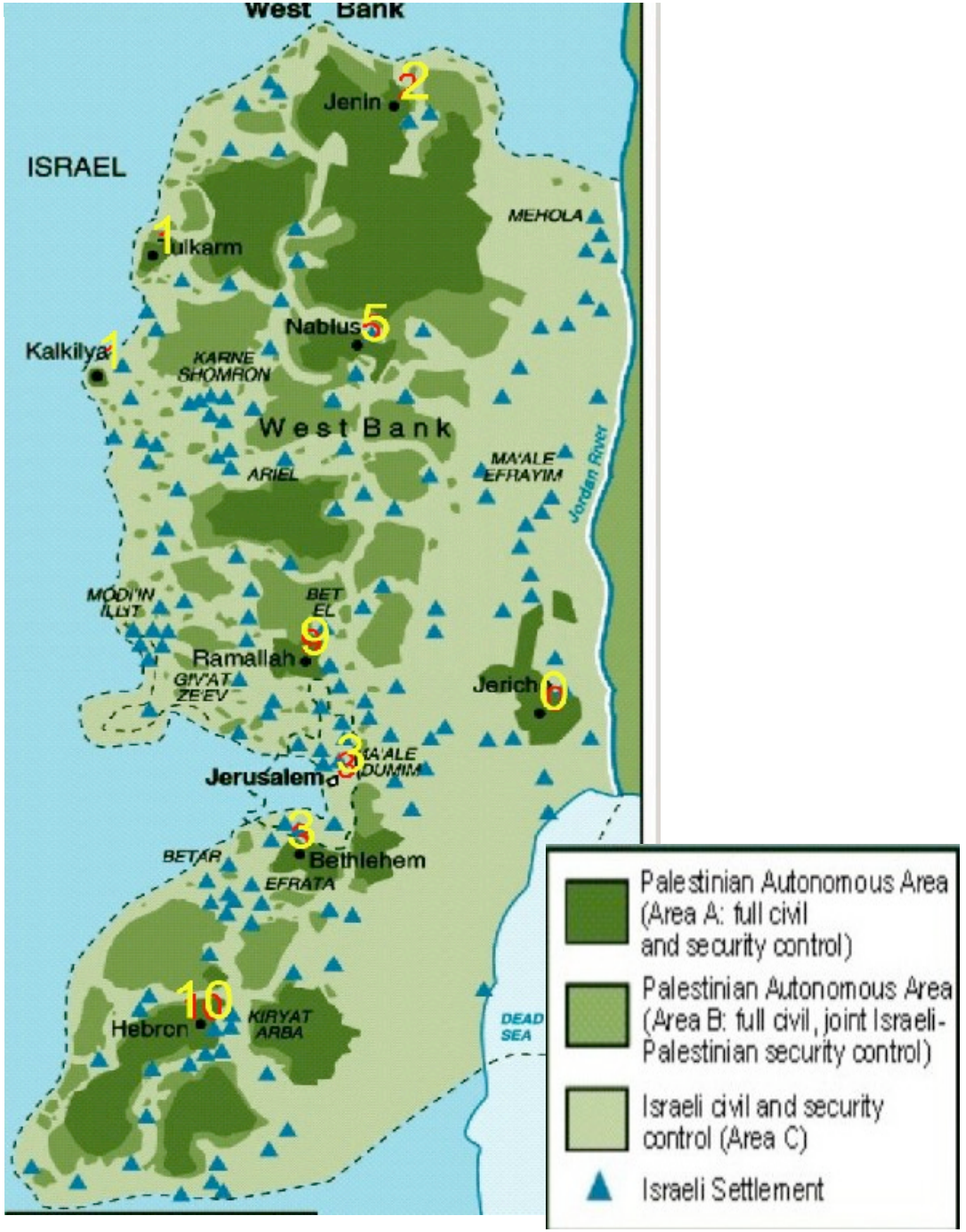
- Although the Palestinian Authority took charge of the health administration , the official efforts done, still did not raise up to the limits of expectation, due to:

  - Lack of medical resources, strategy and expertise.
  - Financial Difficulties.
  - The military checkpoints, closures, and movement restrictions to medical services and civil population.

Distribution of Palestinian Dermatologists in the Occupied Palestinian Territories

WEST BANK (+/- 2.7 million)			GAZA STRIP (+/- 1.5 million)
JENIN	2		+/- 20
TULKAREM	1		
QALQILYA	1		
NABLUS	5		
RAMALLAH	9		
JERUSALEM	3		
BETHLEHEM	3		
HEBRON	10		
JERICHO	0		
TUBAS	0		
JORDAN VALLEY	0		
TOTAL	34		

Among them 7 doctors are working in Palestinian Authority Health Services in outpatient clinics, and other 2 doctors in NGO's services (Medical Relief Committees)



The Palestinian Dermatology

- The Dermatology practice in the Palestinian society is done by private doctors. Recently, the Palestinian Ministry of Health appointed 7 dermatologists in the public sector, and one in the military health services.
- The Medical Union of Doctors in the West Bank of Jordan is still a branch of the Jordanian Medical Union (called the Jerusalem branch, so all the Palestinian territory is represented by one member as any small city in Jordan with less privileges).
- Our society of dermatology (a specialized society of the medical union, was founded in 1996, with 9 dermatologists). Now we have 34 members.

The Palestinian Dermatology

- It is the second year for a new administrative committee of the dermatological society in the West Bank, which began a new era of cooperation among our dermatologist, with clear transparency and responsible accountability in all the activities . So we apologize for our former incompetence to meet the limit of cooperation needed for the TAG project, simply we did not know enough about it.
- From the 27th till the 30th of March this year 2009 our society has succeeded to bring to life our First International Congress of Dermatology, with active high level participation of Arab and International dermatologists.
- The name of our society was changed in our last annual meeting in January 2009 to ”***The Palestinian society of Dermatology***“.

The Medical situation…

- The Medical situation in Gaza Strip is another story , we have never formed (the West Bank and Gaza) 1 medical body, the population was annexed to Egypt before the Israeli Occupation in 1967. And their Medical Union was not integrated in the Jordanian Medical Union for political reasons.

- Until now we have 2 Medical Unions and 2 Dermatological Societies for the same people living in misery since 61 years, under the Israeli Occupation and in the exile.

…is a political issue

- The reason of this introduction is not only to draw your attention to the political aspect and the kind of life we are living, but to tell you that the health status in our occupied Palestinian territories is not only a human, medical or social issue, it is first of all a POLITICAL issue.
- We have an underdeveloped medical capacity with a very exceptional unique socio economically deformed health status. A real competent medical infrastructure is archaic or does not exist , for example we don't have 1 dermatologic section in any hospital, for 4.2 million people.

To be an active TAG partner

- The TAG project needs a special reconsideration in regard to our population, the dermatological body, the facilities on the ground, and the financial possibilities, in addition to the type of administration of this project.

- We hope that by the discussions in this meeting,we can have some ideas and gain from your pilot expertise practical advices of how to begin and how to be an active partner of this project.

A quick overview of our Genodermatoses

- We have all the 6 groups of the severe genodermatoses.
- Having in consideration the high rate of consanguinity in a very closed, besieged, socioeconomically destroyed society, we do not only have the classical Genodermatoses, but some very rare autosomal recessive diseases like the Papular Atrichia (High percentage) the Naxos Disease, the autosomal recessive form of the Ectodermal Dysplasia, some knew entities like the so-called the H- syndrome, and other unknown entities to be identifed.

- We do not have any dermatopathologist,and the biopsy results usually are unconclusive, or missread
- The DNA mapping , is a luxury that we cannot afford it.
- We are here to explain, hear, learn and cooperate with you.

Consanguinity the hidden source of Genodermatoses in the Palestinian society

- Blood relationship because of common ancestry
- Everyone carries rare recessive alleles, (in the heterozygous state), that in the company of another gene of the same type, can cause an autosomal recessive disease.
- The added risks for first cousins mating depend upon their genetic family histories and those risks are *not negligible*.

Genodermatoses

- They represent a large group of inherited single-gene and chromosomal disorders with skin manifestations.
- Many of these disorders are rare. Many are still unknown.
- The recognition of these congenital disorders and their skin findings is important for :
  - The initiation of appropriate dermatologic therapy
  - The detection of other frequently associated multisystem disorders with consequences on the long-term survival and quality of life of the affected individuals.

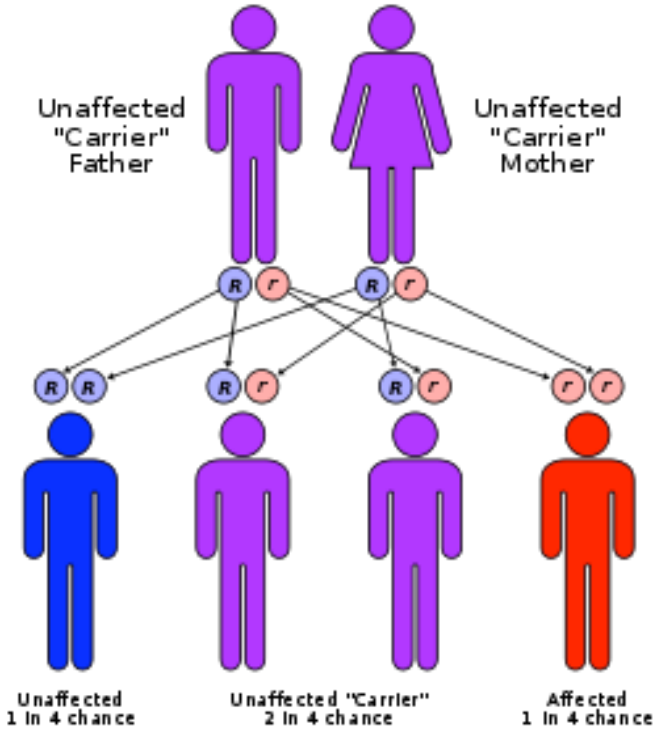
- Our understanding of the pathological and molecular bases of Genodermatoses has improved, but still we lack useful applications to improve the life of the affected.

- Recessive genetic disorders occur when both parents are carriers. As both parents are heterozygous for the disorder, the chance of two disease alleles landing in one of their offspring is 25%.

- 50% of the children (or 2/3 of the remaining ones) are carriers.

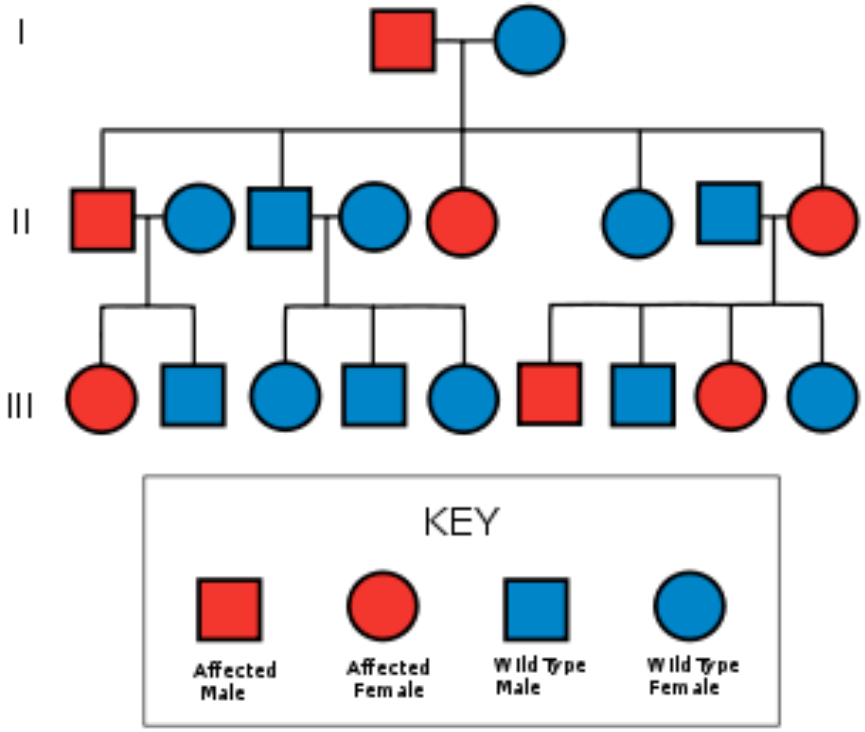
When one of the parents is homozygous, and the other parent is a carrier (a heterozygous). In that case, the chance of disease in the offspring is 50%.

Autosomal recessive allele



An autosomal dominant gene is a *(wild)* gene, the phenotype it gives will be expressed even if the gene is heterozygous

This contrasts with recessive genes, which need to be homozygous to be expressed



Autosomal Dominant Pedigree Chart

- In our Palestinian as in other Arab societies, the in-family marriages are prevailing, we may call it the traditional marriage.
- Most of these marriages are between first cousins, sometimes a double first cousins by both parents sides, and sometimes copied for generations through a well known social deal: "Take my sister, I take your sister"
- In our society, Consanguinity is still considered since hundreds of years as safe, and normal, or even a privilege among cousins.
- It could have been a tribal invention to keep wealth and property within the family, or an **easy,** and i**nexpensive** way of marriage in a closed **conservative**, mainly **rural** society.

- Unfortunately, consanguinity is neither safe, nor healthy; on the contrary it became a terrible burden, a curse, and a threat to our society for generations to come.

- A presentation of some cases of local rare Genodermatoses may prove this opinion right.

Papular Atrichia: a genuine Palestinian Genodermatose

- In two villages, between Bethlehem and Hebron (in a 20 sq. Km) hundreds of persons are affected with a rare autosomal recessive syndrome known as *Papular Atrichia.*

- It may be the highest incidence of this condition in the world: we may call it a genuine Palestinian Genodermatose.

Papular Atrichia

OMIM#209500

- An autosomal recessive disorder characterized clinically by the occurrence of universal congenital alopecia and disseminated papular lesions.

- Recently, mutations in the human hairless (HR) gene have been reported in Irish and Arab Palestinian families with papular atrichia, J Invest Dermatol. 2000 Oct;115(4):761-4.

Papular Atrichia

OMIM#209500

- Babies with PA are born with hair and is completely lost before the age of two months
- Except one Palestinian baby girl still having some hair at 3 years of age, genetically confirmed to have the same mutation (?? Subtype ??)

Ectodermal Dysplasias (ED)

- Comprises a large, heterogeneous group of inherited disorders that are defined by primary defects in the development of two or more tissues derived from embryonic ectoderm.
- The tissues primarily involved are the skin, hair, nails, eccrine glands, and teeth.
- Collectively, the International prevalence of ectodermal dysplasia is estimated at 7 cases per 10,000 births

Ectodermal Dysplasias (ED)

The most common ectodermal dysplasias are:

- X-linked recessive hypohidrotic ectodermal dysplasia (Christ-Siemens-Touraine syndrome)
- X-linked hidrotic ectodermal dysplasia (Clouston syndrome).

Ectodermal Dysplasias (ED)

- The existence of a rare autosomal recessive form was first reported by Gorlin et al. (1970) of a female with the HED syndrome with parental consanguinity.
- **Munoz et al.** (1997) identified 5 families with autosomal recessive HED.
- **Kabbaj et al.** (1998) reported a large consanguineous Moroccan family in which 14 individuals, both male and female, were affected.
- **Shimomura et al.** (2004) reported a 24-year-old Japanese woman with autosomal recessive HED
- The only type of ectodermal dysplasia seen in my clinic is the rare type of this disorder, the Autosomal Recessive Hypohidrotic Ectodermal Dysplasia . The patients in this presentation have other males and female family members affected, but with normal parents, mostly cousins. The first case seen in 2004 was referred from Hebron by my colleague Dr.Maraqa. He did suggest Christ-Siemens-Touraine syndrome and it was really an ectodermal dysplasia.

Epidermolysis Bullosa

- Epidermolysis bullosa (EB) is a clinically and genetically Heterogeneous group of blistering skin diseases.

- Based on ultrastructural analysis of skin biopsies, the main types are designated as:
  - Simplex,
  - Junctional,
  - Dystrophic

Epidermolysis Bullosa

- EB simplex, a dominantly recessive type causes recurrent, non-scarring blisters from increased skin fragility.
- Junctional EB is characterized by extreme fragility of the skin and mucus membranes with blisters occurring after minor trauma or friction (both lethal and non-lethal autosomal recessive forms exist)
- In Dystrophic EB, the blisters cause mutilating scars and gastrointestinal strictures, there is an increased risk of severe squamous cell carcinomas in affected individuals.(Autosomal recessive and dominant cases caused by mutations in the collagen VII gene.)

Xeroderma Pigmentosum

- XP is a rare autosomal recessive disease, first described by Kaposi in 1870

- Characterized mainly by:
  - Photosensitivity, (Freckles, and moles.)
  - Pigmentary changes,(spots of various tints of brown.)
  - Premature skin aging, (atrophic patch and telengectasia.)
  - Neoplasia (Actinic keratoses, Kerato-acanthomas, melanomas and squamous cell carcinoma are later manifestations.
  - Abnormal defect in DNA repair (Vesiculobullous lesions and superficial ulcers, healing with difficulty)

Ichthyosis

- A relatively uncommon group of skin disorders characterized by the presence of excessive amounts of dry surface scales
- It is regarded as a disorder of keratinization or cornification, and it is due to abnormal epidermal differentiation or metabolism
- Ichthyosis vulgaris is the most common form and is an autosomal dominant trait.

Ichthyosis

- Epidermolytic hyperkeratosis, is an autosomal dominant disorder.
- Lamellar ichthyosis, a more severe form of dermatosis, is an autosomal recessive trait.
- X-linked ichthyosis, an autosomal recessive trait.

The recognition of these Genodermatoses,
mostly the autosomal recessive types,
can help through
primary health education
and medical genetic counselling,
to uncover the awful consequences of
traditional in-family marriages in our society,
with less genetic victims,
and less human sufferings.