Noninfectious diseases in the tropics

General considerations 1.

- All kind of the diseases are found in the tropics, but their prevalence and appearence can be different.
- The prevalence of the so called „western” diseases (diabetes, hypertonia, obesity, etc.) are increasing.
- Alcoholism, smoking and the use of narcotics are inreasing also.
- Due to industrialisation environmental pollution (lead) appeared.

Cardiovascular diseases 1.

- Hypertension: according to WHO criteria (≥160 Hmm systolic, ≥95 Hgmm diastolic) the prevalence of the hypertension in certain african countries ranges between 5-10%, strongly associated with obesity, diabetes and the socio/economic status.
- The clinical symptoms are similar to other countries.
- In african blacks the plasma renin/angiotensin II level is low, and the efficacy of the ACE inhibitors in reducing the blood pressure are limited.
- In certain asian populations the frequency of obesity and glucose intolerance is increased among hypertensives.

Cardiovascular diseases 2.

- **Ischaemic heart disease: the incidence is increasing in the tropical countries and strongly associated with obesity, diabetes, alcoholism and smoking.**
- **Certain racial differences can be observed. It is low in african countries, but relatively high among the population of indian origin. In chinese people, the incidence is 4-8 lower, than in whites.**

Cardiovascular diseases 3.

- **Rheumatic heart disease:** the appearence of the disease is associated with poor hygienic and crowded condition and poverty.
- The prevalence of the disease in children is 1/1000 (WHO).
- Out of every 100 sore throat 20 is caused by *Streptococcus pyogenes* in tropical countries. Out of every 100 *S pyogenes* infection 20 will be associated with fever and cervical lymph gland enlargement and out of them 2 will develop into rheumatic heart disease. Out of the remaining 80% asymptotic infection 1 will develop into rheumatic heart disease.

Cardiovascular diseases 4.

- **Endomyocardial fibrosis (EMF): the EMF is a charasteristic disease in tropical countries and associated with the circular fibrotic thickening of heart ventricles. The fibrotic process starts from the apical region and spreads to the valvular muscles producing mitral incompetence (insufficiency).**
- **The development of the disease is associated with the hypereosinophilia, frequently observed in tropical countries due to different parasitic infections (filariasis).**

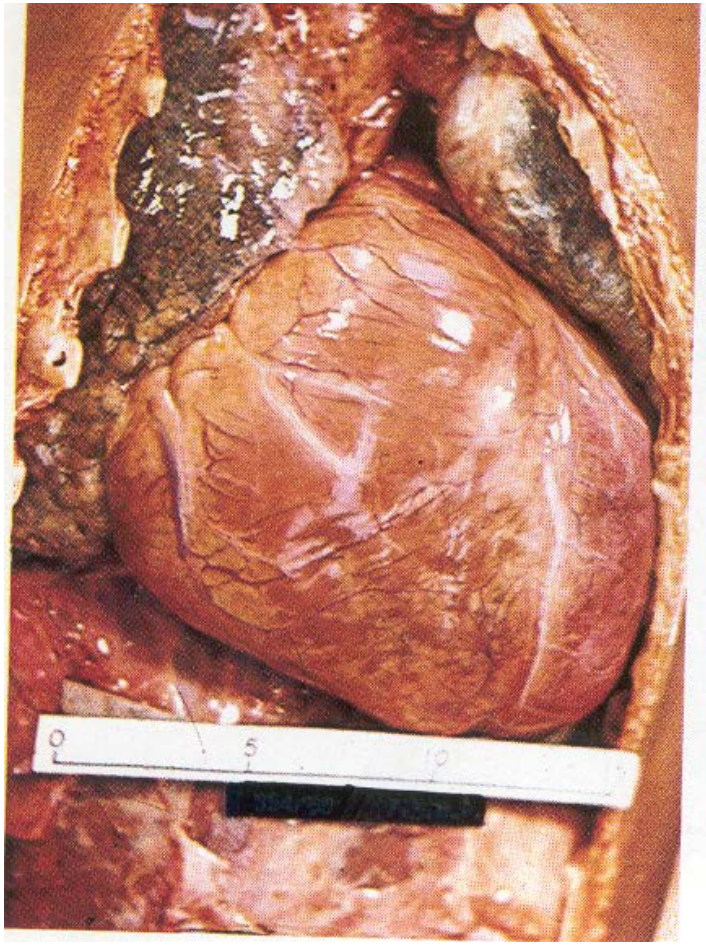
Cardiovascular diseases 5.

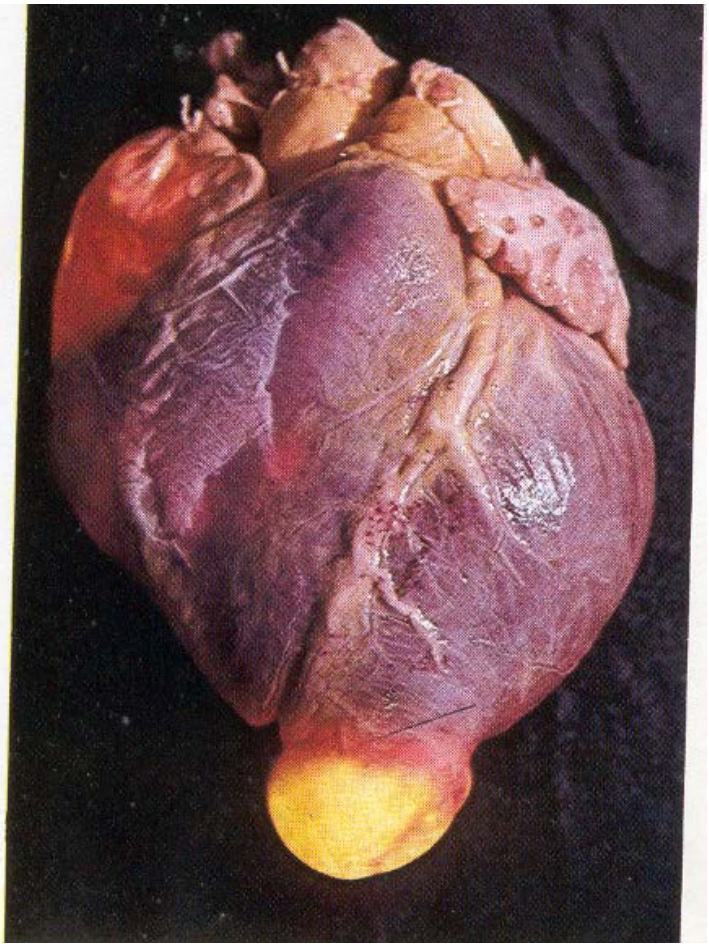
- Peripartum cardiac failure (PPCF): cardiac failure develops during pregnancy in multipara women, or within 6 month after delivery. The disease generally disappeares shortly after delivery. The exact etiology in not known. Dilatative cardiomyopathy develops.
- No specific treatment.

Cardiovascular diseases 6.

- **Cardiac disease of parazitic origin:**
- ***Trypanosoma cruzi* infection produces the Chagas' disease. It develops frequently 20 years after the infection.**
- ***Toxoplasma myocarditis:* develops in AIDS.**
- ***Trichinosis:* associated with high fever, eosinophilia, cardiac failure, arrhytmia, muscle pain.**
- ***Cysticercosis and hydatid disease***
- ***Schistosomiasis***
- ***Other parazitic infections (Trypanosoma rhodesiense, gambiense).***

Chagas-disease





Cardiovascular diseases 7.

- **Pericarditis: the occurence of the pericarditis in tropical countries is generally associated with other serious bacterial infections, or tuberculosis. The symptomatology depends on the volume and the speed of the accumulation of fluid in the pericardial sack. In the case of quick accumulation, the developing symptoms are very serious with dyspnoe, pulsus paradoxus and cardiac tamponade. The immediate puncture of the pericardial sack is life saving. In HIV infected patients the tuberculotic origin of the pericarditis is frequent.**

Cardiovascular diseases 8.

- **Cardiomegaly of different origin: cardiomegaly is not rare among children living in tropical countries. The etiology of cardiomegaly remains unknown in several cases. Few of the etiologies are listed below:**

a. Malnutrition (Kwashiorkor)

b. Myocarditis of different origin

c. Parazites

d. Cardiomegaly of alcoholic origin

e. B1 vitamin deficiency

Diabetes

- **The prevalence of insulin dependent diabetes mellitus (IDDM), type I. diabetes) is about 2,2/1000 in Finland, 1 in the USA, 0,03 in Japan, 0,03 in Africa.**
- **The prevalence of non inzulin-dependent diabetes mellitus (NIDDM, type II. diabetes) in Europe and in the USA is 2-4%, in the Indian subcontinent is 7%, among pima indians and micronesia (Naura island) 50%. Among black africans is 1%.**
- **Diabetes mellitus, different from type I. and II. diabetes mellitus can be found in tropical countries. This type requires phasicly large amount of insulin and related malnutrition (MRDM). According to WHO classification this group can be subdivided into protein deficient diabetes mellitus (PDDM) and fbrocalculosus pancreatic diabetes (FCPD) groups. The pathomechanism is not known.**

The occurence of malignancies

- **Tropical countries**
  - **Uterus cervix**
  - **Stomach**
  - **Oropharynx**
  - **Oesophagus**
  - **Breast cancer**
  - **Lung**
  - **Liver**
  - **Colorectal tumors**
  - **Lymphoma**
  - **Leukemia**
- **Industrial countries**
  - **Lung**
  - **Colorectal tumors**
  - **Breast cancer**
  - **Stomach**
  - **Prostatic cancer**
  - **Bladder**
  - **Lymphoma**
  - **Oropharynx**
  - **Uterus corpus**
  - **Uterus cervix**

Haemoglobinopathies

Structure of haemoglobin 1.

- **Definition:** The haemoglobins are a group of related proteins (*globins*) to each of which the same prosthetic group, *haem* , is attached.
- **Haem:** The iron atom at the centre of haem is normally in the ferrous state (Fe++). If at any time the iron atom becomes permanently oxidised to ferric form (Fe+++) the „haem" becomes haematin. This process takes place if *water molecules* are excluded from the region.

Structure of haemoglobin 2.

- **Globin:**
- Primary structure: the specific amino acid sequence of each individual polypeptide chain
- Secondary structure: the coil formation (alpha -helics).
- Tertiary structure: the twist and turn of the helix (for stability).
- Quaternary structure: the molecule shrinks on oxygenation and expands on deoxygenation (paradoxical breathing).
- **Th haem is embedded into the globin part of the molecule surrounded by water repellent-hydrophobic-amino acid residues (proximal-distal histidine).**

Structure of haemoglobin 3.

- **<u>Man has at least four physiological haemoglobins (</u>** Adult: HgbA, $HgbA_2$, Fetal Hgb, Embrionic Hgb**)**
- Amino-acid substitustion in any of the globin chains alters the properties of the haemoglobins.

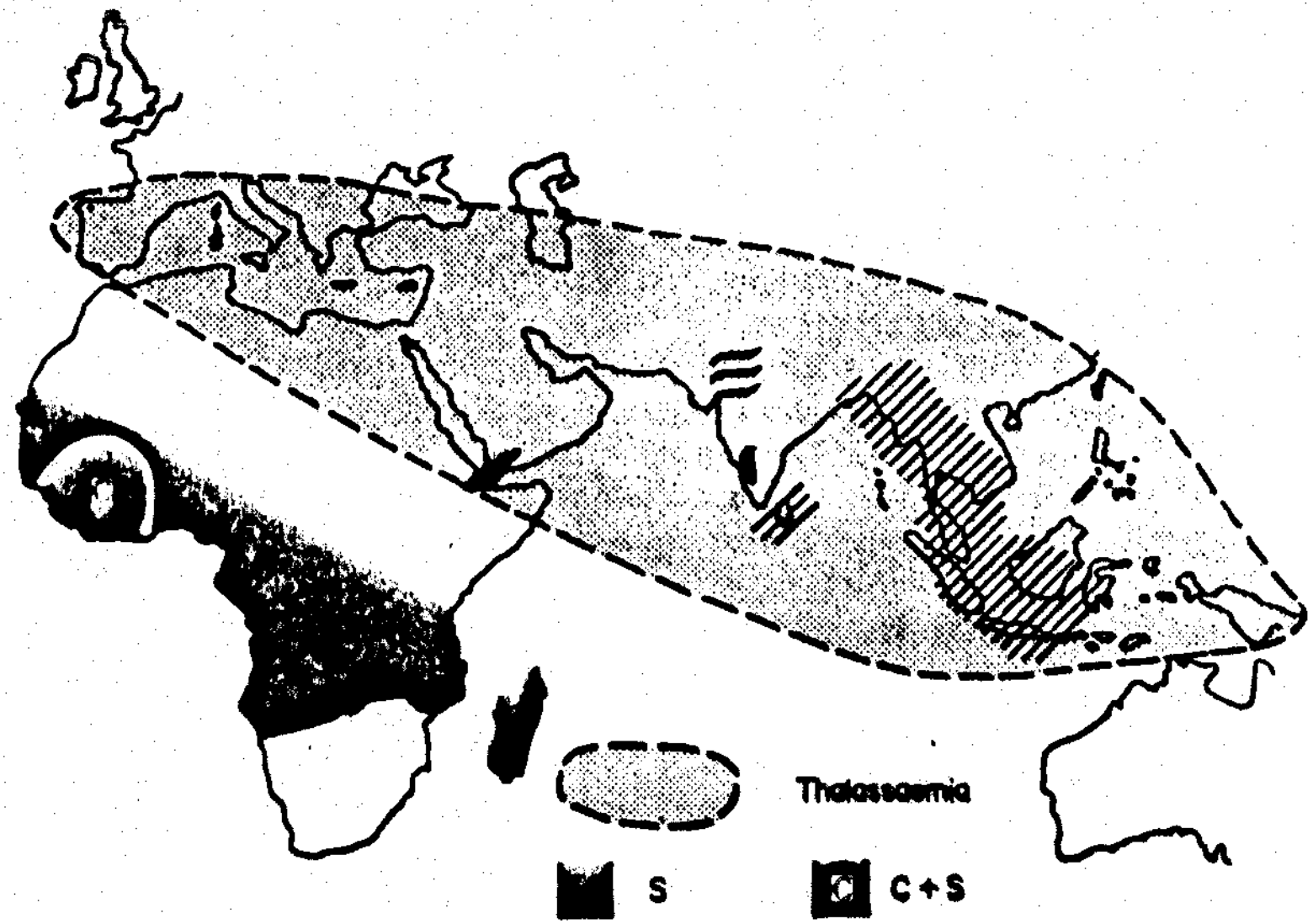
Diminished alpha and beta chain production (either complete or partial) is called thalassaemia.

The substitution of valine for glutamic acid in the sixth position of the beta - chain called haemoglobin S (other types of substitutions might develop as well).

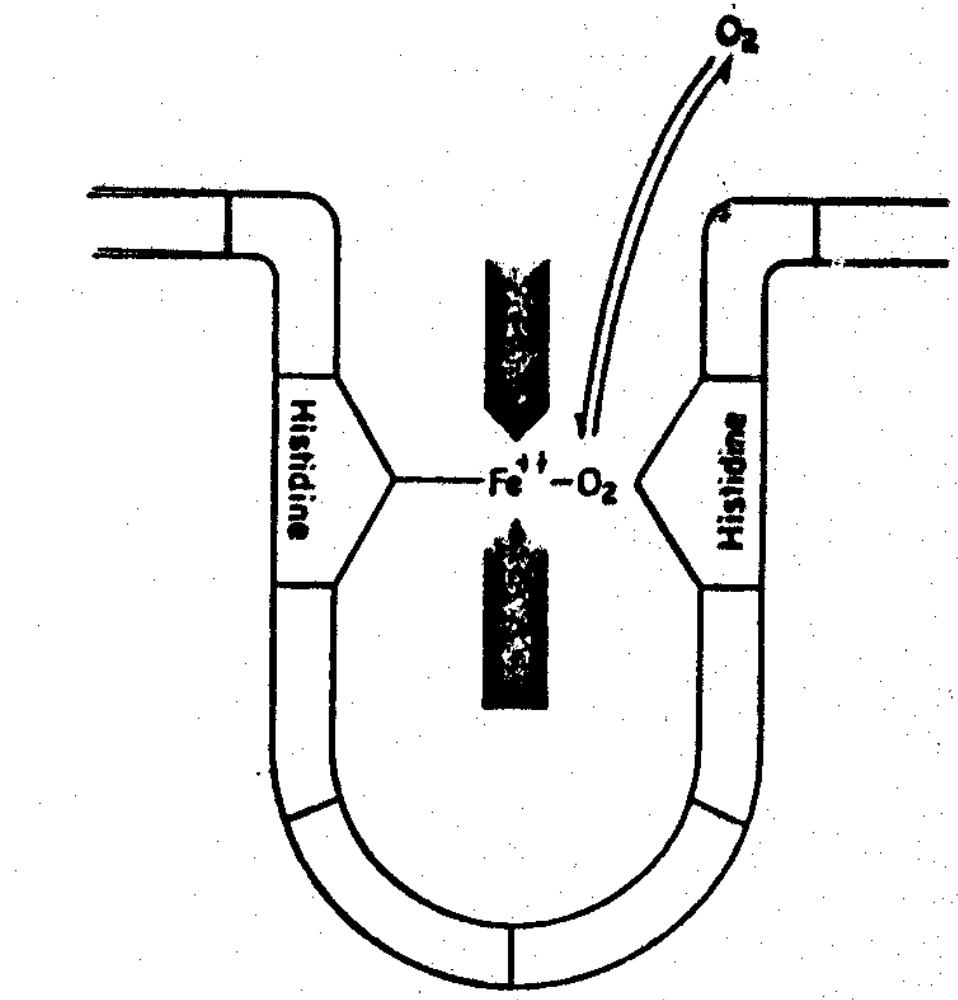
Normal haemoglobins

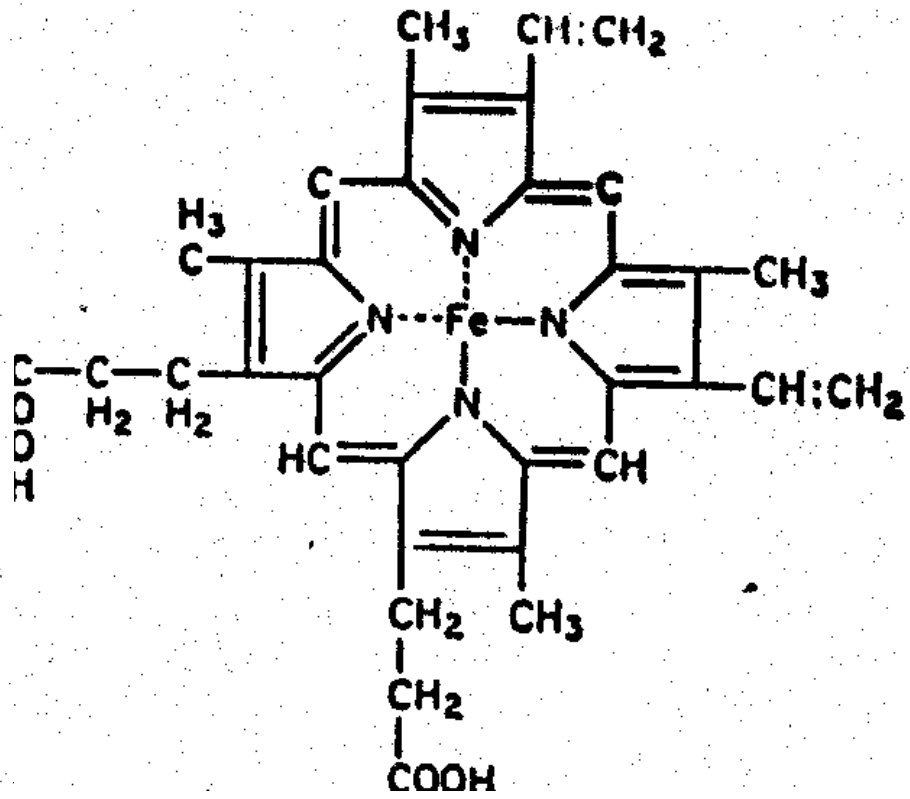
- **Adult haemoglobin (alpha 2-beta 2, hgb A)** comprises about 98% of haemoglobin of the adult
- **Haemoglobin A2 (alpha2-delta2)** is a small fraction of the total adult haemoglobin
- **Fetal haemoglobin (hgb F, alpha2-gamma2)** which forms the 80% of the hgb of the newborn in the first few month
- **Embrionic haemoglobin (hgb Gower, alpha2-epsilon2)** which is found only during the first 3 month of intrauterin life
- **Because of the above haemoglobins contain two alpha chains , they are half alike, it is in the second half that they differ.**

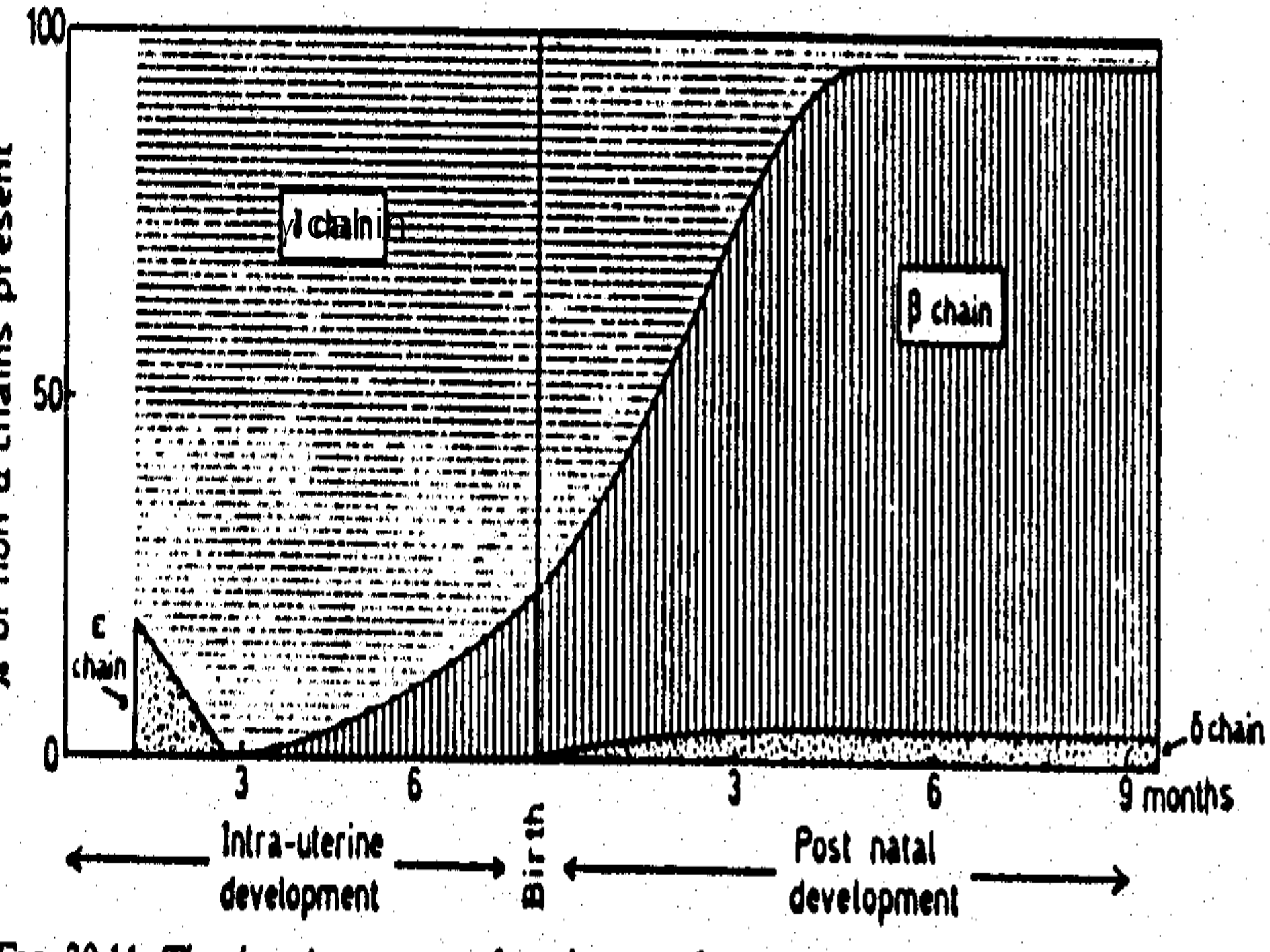
The distribution of haemoglobinopathies



The structure of haemoglobin






100
50
0
γ chain
β chain
ε chain
δ chain
3
6
3
6
9 months
Intra-uterine development
Birth
Post natal development

Diminished alpha - and beta chain formation (alpha and beta thalassemia)

- Thalassaemia may exist in homozygous (major) and heterozygous (minor) form
- Severe depression of beta chain production is called **beta thalassaemia major**
- In **alpha thalassaemia** the beta chains are formed in tetramers solely of beta- gamma chains (hgb H)

Beta thalassaemia (clinical signs) 1.

- **Beta thalassaemia major:**

1. Homozygous state for beta thalassaemia (no hgb A production)
2. The child presents with anaemia of increasing severity (splenomegaly and hepatomegaly develops)
3. There is a compensatory hyperthrophy of the bone marrow, which is common to all congenital haemolytic anaemias (this can be demonstrated on X-ray)
4. Due to repeated transfusions iron overloading and cardiac failures develops

Beta thalassaemia (clinical signs) 2.

- **Beta thalassaemia minor**

1. This is the heterozygous state for beta thalassaemia
2. The degree of anaemia is highly variable (iron resistant anaemia)
3. Hepato-splenomegalia develops
4. The patients with this condition are able to live and work

Alpha thalassaemia

- **Alpha thalassaemia major** is incompatible with life
- **Alpha thalassaemia minor:** the heterozygous state for alpha thalassaemia. That carriers are perfectly fit, only minimal microcytosis can be present
- **Haemoglobin H disease:** the mode of inheritance is uncertain. Only beta chains are produced. The clinical signs are similar or somewhat more severe than that typically found in beta thalassaemia

Abnormal haemoglobins (S, C, D, E)

- **Definition:**The common hgb variants all result from the amino acid substitution in the beta chain
- **Hgb S:** substitution of valin for glutamic acid in the 6-th position of the beta chain
- **Hgb C:** substitution of lysin for glutamic acid in the 6-th position of the beta chain
- **Hgb D (Punjab):** substitution of glutamine for glutamic acid in the 12-th position of the beta chain
- **Hgb E:** substituion of lysine for glutamic acid in the 26-th position of the beta chain

Sicle cell anaemia 1.

- This is the homozygous state for haemoglobin S and the most severe form of the disease
- **The pathomechanism: the altered hgb becomes labile and easily cristalliyse within the red cell, resulting in destortion of the red cell shape**
- Clinical features:

1. Appearence: short trunk with comparatively long legs and asthenic built
2. Pale mucous membranes, slight jaundice
3. Leg ulcers or scars of past ulcers
4. Hepatomegayly is present,but splenomegaly is rare over 3 years of age
5. **Sicle cell crises can be *aplastic* with serious anaemia, when the blood formation stops due to exhausted bone marrow or *occlusive***

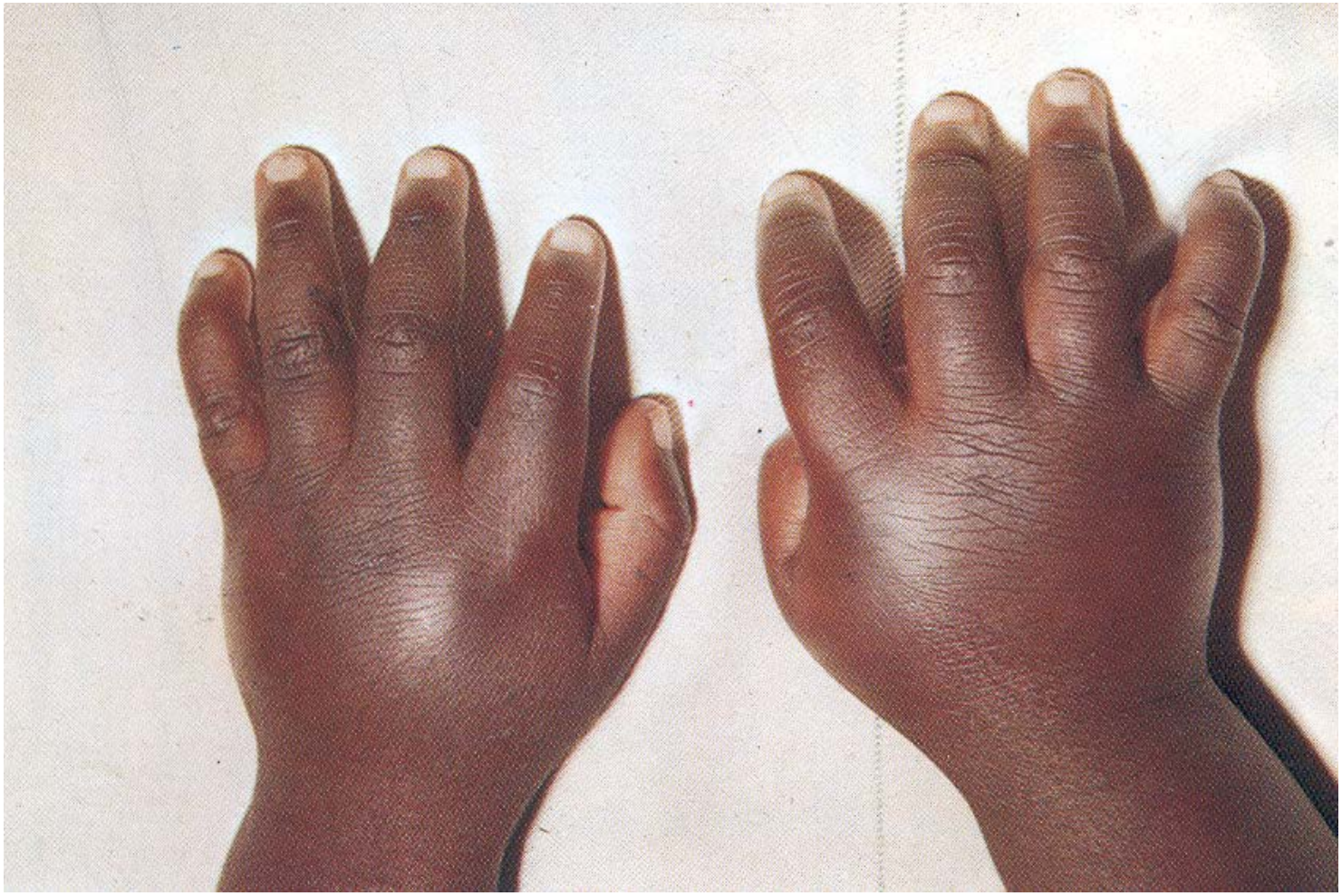
Sicle cell anaemia 2.

- **Occlusive crises**: The crystallised hgb S produces the „sicle cell" shape of the red cells, which are producing the occlusion of the small vessels. The occlusive crisesmay occur at any site of the body and account for multiple manifestations of sickle cell anaemia.
- **The clinical signs of the ooclusive crises 1:** In children bones appear to be particularly affected and this may mimic osteomyelitis or rheumatism , dactilytis with swollen painful fingers. Patients bony manifestations are particularly labiliable to salmonella infections.

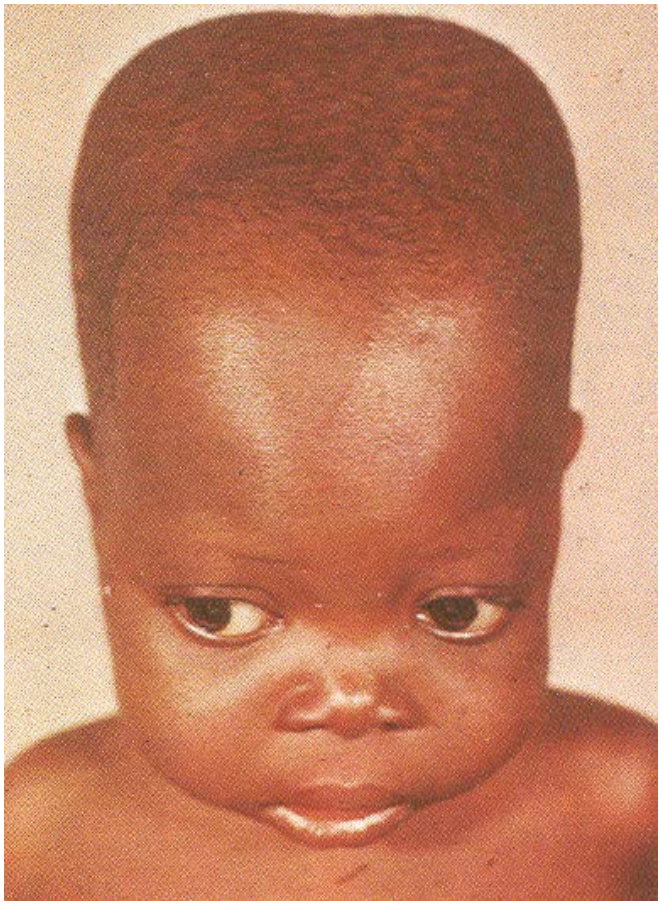
Anaemic crisis

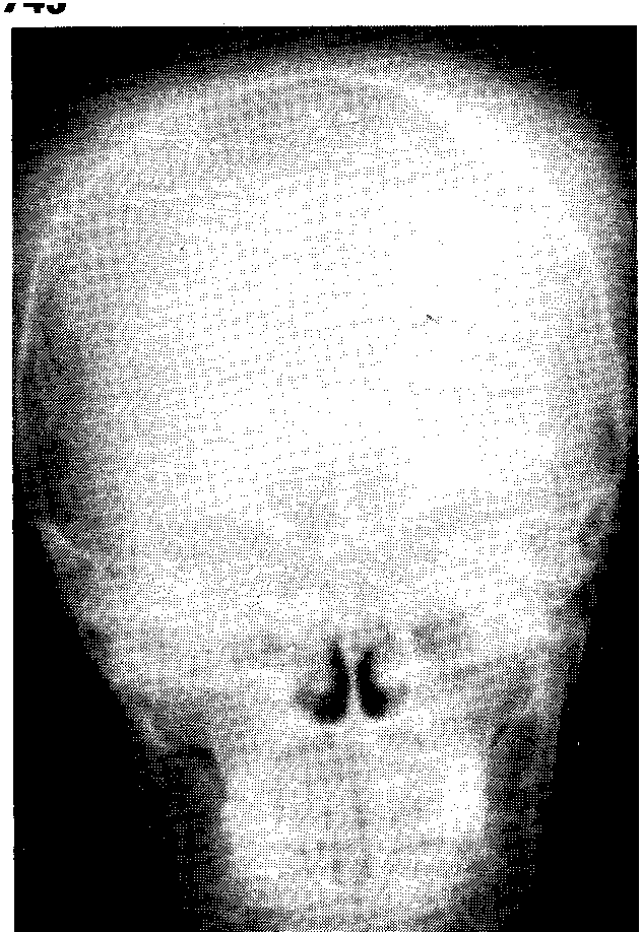
- The main feature: is the catastrophic declines of Hgb are the result of malaria, acute splenic sequestration, folate deficiency and aplastic crisis.
- Malaria is always associated with the most severe anaemia.
- The sequestration crisis is characterised by an acutely enlarging spleen and a sudden fall of hgb level.
- The folic acid deficiency is more frequent in pregnancy.
- Any acut infection (viral infection) can precipitate aplastic crisis.

Dactilitis in sickle cell disease



Scull changes in sickle cell disease





Treatment possibilities 2.

- Management the patients in crisis (control of pain, restoration and maintenance of hydration, treatment of infection).
- Antiinfective treatment indicated (exclude malaria): fever over 39 C°, acute pulmonary syndrome, suspected meningitis.

Treatment possibilities 3.

- Cerebrovascular accidents: patients should be treated individually.
- Priapism: Treatment is aimed at relieving pain. In mild cases cold water, mixturition, walking around might help. In serious cases the viscous blood should be aspirated under spinal anesthesia.
- Management during pregnancy: prophylactic antimalarials and folic acid provided. Transfusion is given if delivery starts with 80g/l hgb.

Treatment possibilities 4.

- **New treatment: Hydroxyurea or butyrate therapy increase the proportion of HbF and reduces the intracellular polymerization of HbS and haemolysis: results of extensive and controlled trials are awaited. Slected patients have been cured by bone marrov transplantation.**

Protein calorie (energy) malnutrition (PEM) of early childhood

Nutritional requirements in the tropics 1.

- Energy requirement for an adult man of 25 years is 3200 calories (1300 kJ)/die on temperate zone.
- On hot climates this requirement is about 10-20% less.
- It has been estimated, that some villagers consume only 2040 calories (8500kJ)/die and are permanently hungry.

Nutritional requirements in the tropics 2.

- Pregnancy and breast feeding increase the energy requirement. For one baby for the first 6 month the mother require 600 calories extra.
- Diets in the tropics are unbalanced and deficient in calories. For those consuming 2040 calories/day, the daily intake includes only 53g protein of which only 6 g are of animal protein.

Definition

- This constitutes the most widespread and serious nutritional public health problem in the world.
- It can be devided to **kwashiorkor and marasmus.**
- Three interrelated biological stages can be differentiated: intrauterine fetus, the extrauterine fetus (the first 9 month of life) and transitional life (up to 4/5 years).

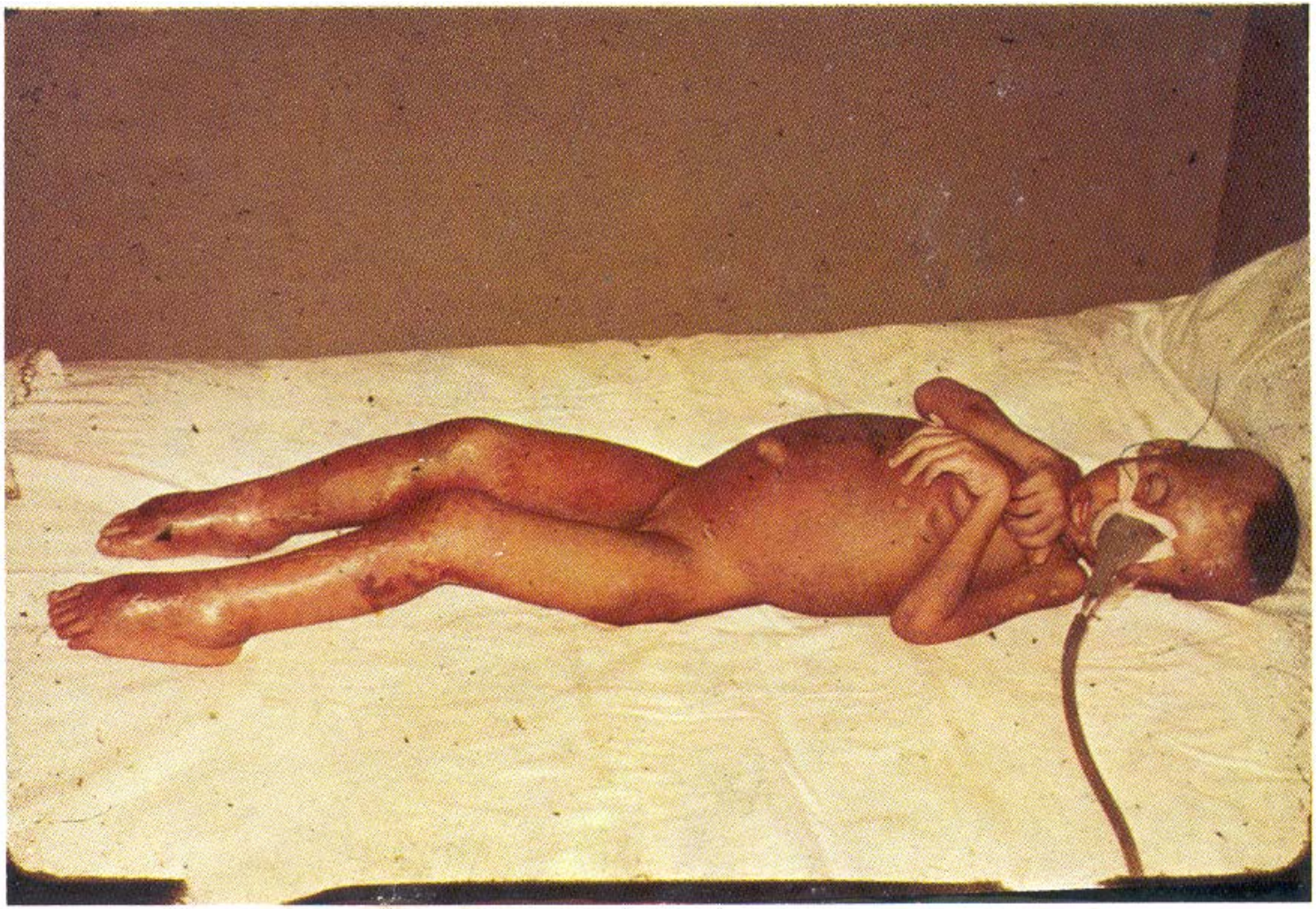
Kwashiorkor 1.

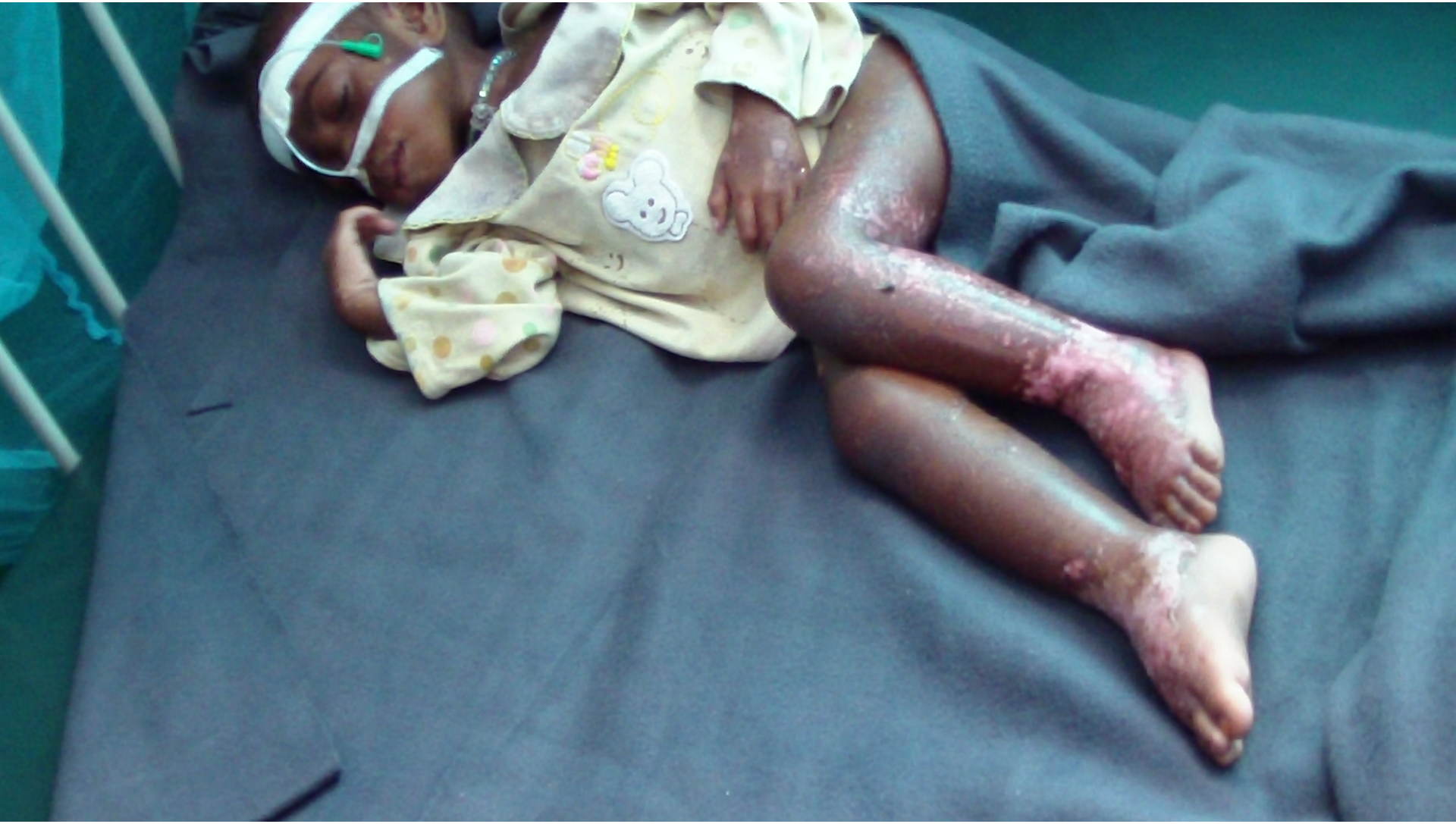
- Definition: **kwashiorkor** is one of the most severe syndrome of early childhood. It is most frequent in the second year of life. It is due to an imbalanced diet which is very low in protein but contains carbohydrate calories, associated with a variable burden of microbial and parasitic infections and psychosocial factors.

Kwashiorkor 2.

- Clinical features:
  - oedema
  - Growth failure
  - Psychomotor change
  - Wasted muscles with retention of some subcutaneous fat.
- ***The features are called the kwashiorkor tetrad.***

Kwashiorkor





Kwashiorkor 3.

- **Etiology:**
- **The primary cause is always an imbalanced diet, low in protein, but sufficient in carbohydrate calories.**
- **In traditional communities is mainly a disease of the secotrant (the child in the second year of life).**
- **The breast feeding is being stopped and other foods consist of low protein.**
- **The non-immune child is exposed to a wide and cumulative burden of infections.**

Kwashiorkor 4.

- The reasons of protein deficient diet:
  - Poverty
  - Lack of knowledge
  - Incorrect knowledge
  - Infections
  - Psychosocial factors

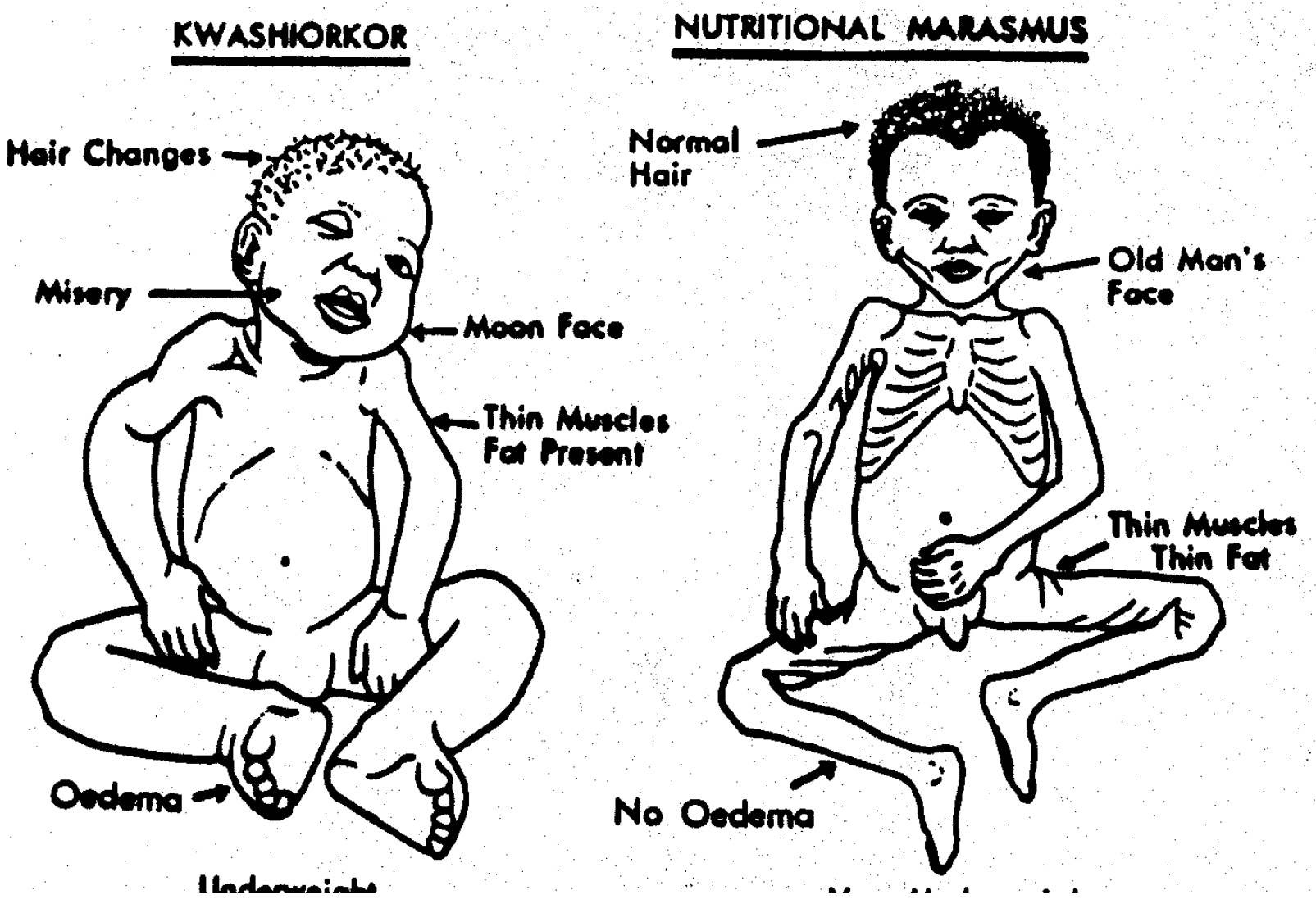
Kwashiorkor 5.

- **Pathophysiology:**
  - **The organism main turn-over rate of protein are effected**
  - **The slowing growth is the most important adaptive function**
  - **The liver is enlarged with fatty degeneration**
  - **The pancreas is atrophic**
  - **The small intestine is thin-walled**
  - **Steatorrhea**
  - **Haematopoesis in infterferred with (due to protein, iron and folic acid deficiency).**
  - **Enzyme systems are affected.**
  - **The potassium and magnesium stores of the body are greatly depleted.**

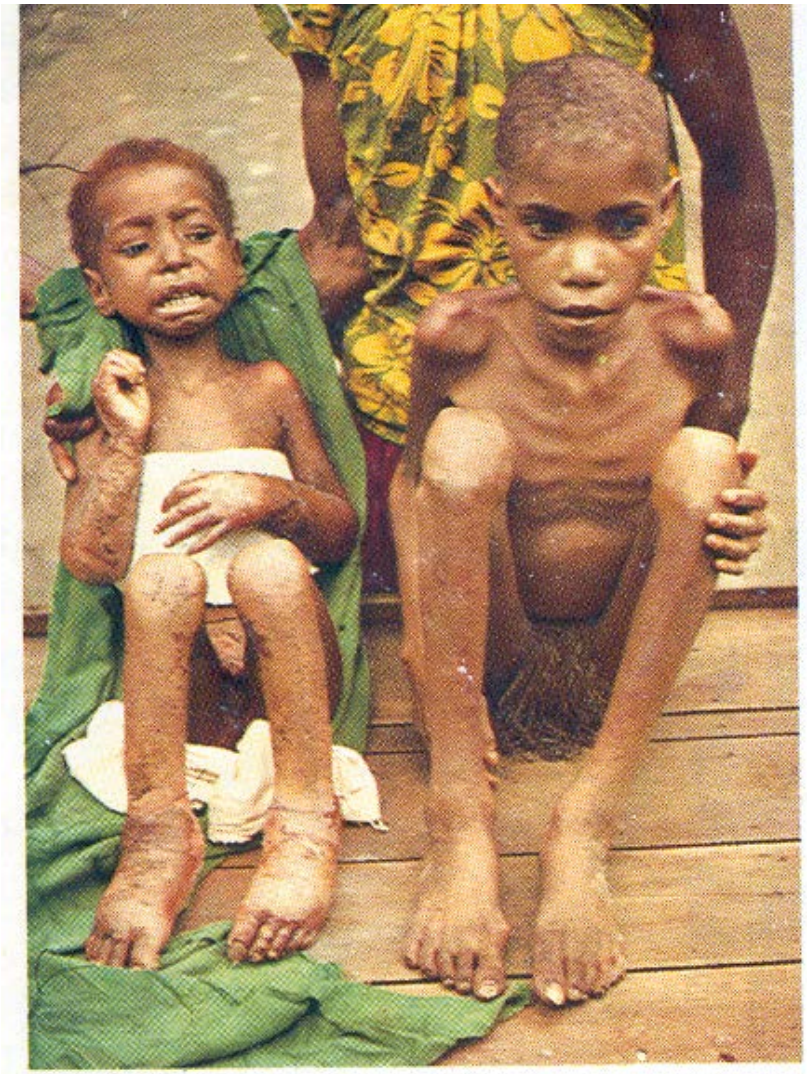
Kwashiorkor 6.

- **Symptomatology 1.**
  - **Constant:**
    - **Pitting oedema of the legs**
    - **Growth failure (usually below 80%)**
    - **Psychomotor change of complex etiology**
    - **Muscle wasting with some overlying subcutaneous fat**
  - **Usual:**
    - **Hair changes (flag signs, dyspigmentation, easily pluckable).**
    - **Anaemia**
    - **Diarrhoea**
    - **Moon/face**

Kwashiorkor and marasmus



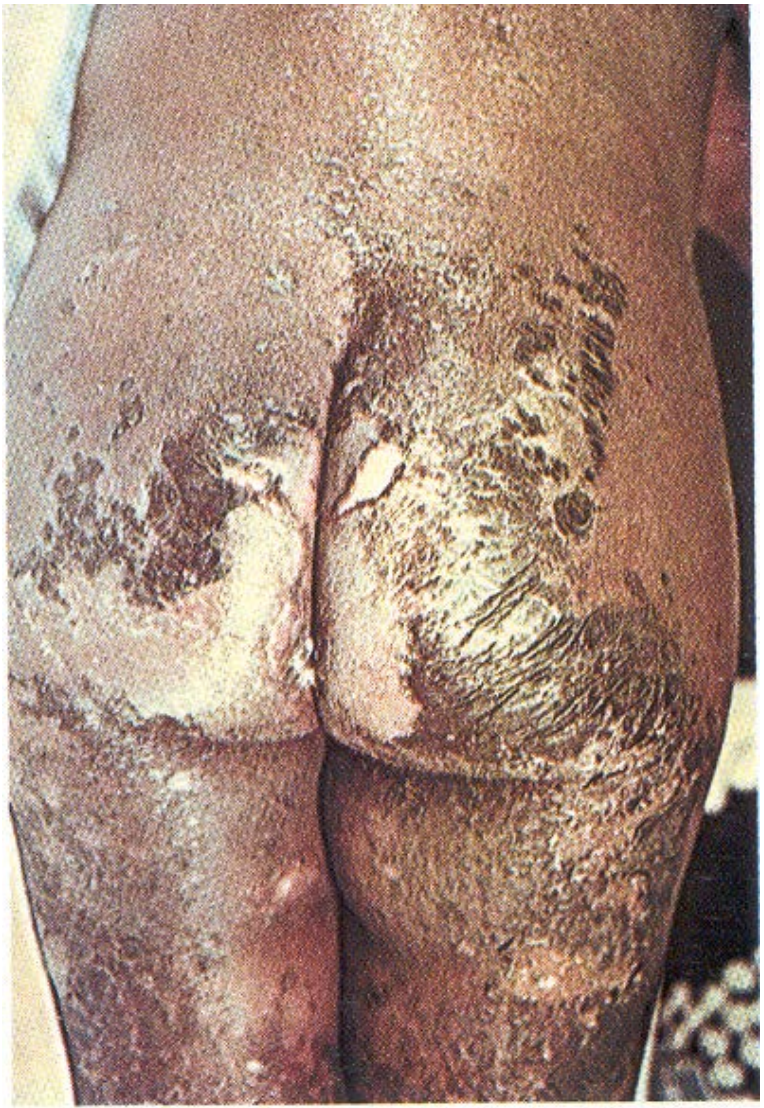
Kwashiorkor and serious marasmus



Kwashiorkor 7.

- Symptomatology 2.:
  - Occasional:
    - Hepatomegaly
    - Skin lesions: indolent stores, groin rash, flaky - paint rash
    - Signs of associated infections
    - Associated vitamin deficiences

Skin changes in kwashiorkor



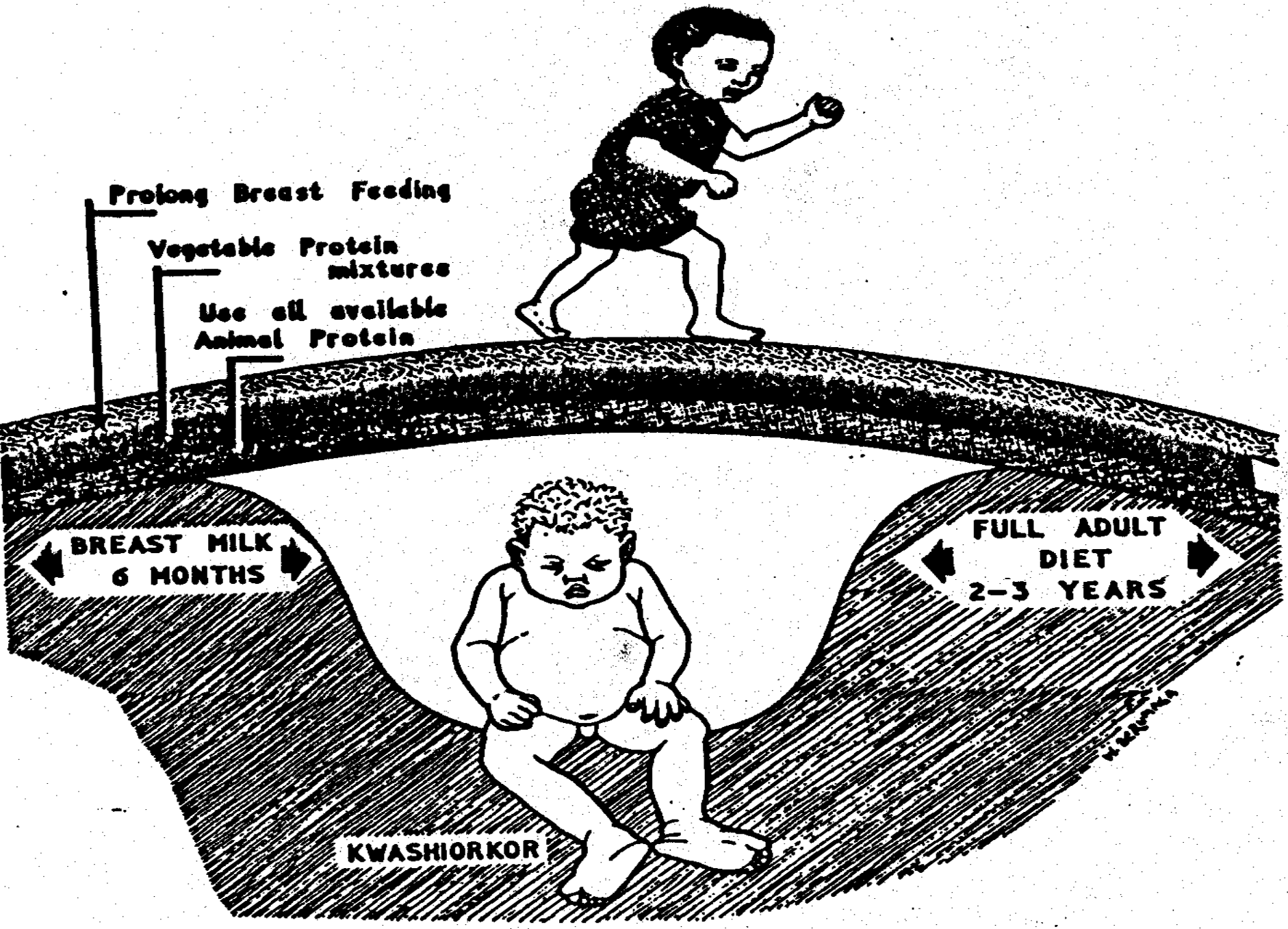


FIG. 27.8. *Three plank protein bridge.*

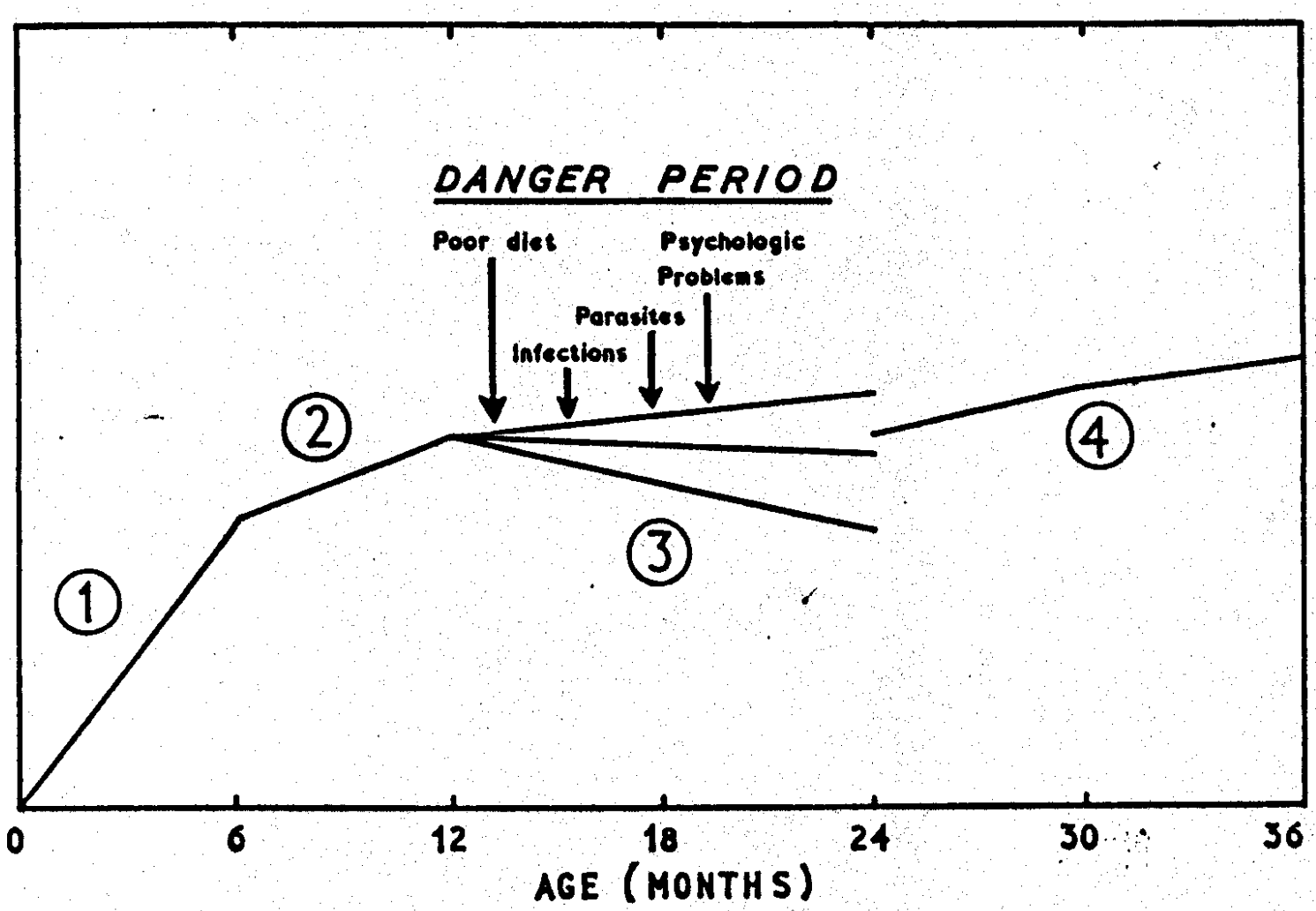


FIG. 27.1. *Typical weight curve in early childhood in tropical regions.*

Kwashiorkor 8.

- **Treatment 1.:**
  - **Diet: 4g/kg protein, 100 cal/kg and adequate potassium, magnesium.**
  - **Liquid food is provided (125ml/kg/die).**
  - **Vitamins, minerals should be supplemented (vitamin A 10000 IU for 7 days, folic acid 5 mg/die, ferrous sulphate 300 mg/die).**
  - **Treating infections (worms, tuberculosis etc.)**
  - **Treating dehydration (150ml/kg/die)**
  - **Treating hypothermia, hypoglycaemia is important (could be the reasons of sudden death).**

Kwashiorkor 9.

- **Treatment 2.:**
  - **The basis of treatment is skimmed milk powder (50g) which can be used with calcium caseinate (50g), sucrose (20g) and cottonseed oil (30g) in water to 1 litre.**
  - **Total intake: 120/140 calories (500/600 kJ)/kg/day.**
  - **Lactose free nutrient: groundnut 150g, wheat flour 50g, maize flour 100g, cottonseed oil 25g and sucrose 75g formed into biscuits.**

Pathology 1.

- Liver: fat appears in the periphery of the lobules and later involves the centre as smalld droplets which coalesce.
- Pancreas: pale and atrophic. Vacuolization can be observed. Calcification can occur.
- The salivary glands: show marhed atrophy with loss of acinary cells.

Pathology 2.

- **Gastrointestinal tract: the enzyme-secreting cells of the mucosa are atrophied. Blunting and broadening of the villi observed. Due to the loss of disaccharides, lactose and glucose intolerance develops.**
- **Heart: the heart is small and atrophied with histological and biochemical evidence of myocardial dysfunction.**

Pathology 3.

- **Thymus: the thymus is atrophied; this is related to the immundepression evident in PEM.**
- **Brain and central nervous system: the wight if the brain is decreased. Atrophy, vacuolization observed. There are degenerative changes in the central ganglia, with reduction in the size of cortical neurons**

Pathology 4.

- Skin: The skin shows hyperpigmantation with subsequent exfoliation, atrophy, hypopigmentation and combination of ulcers, fissures, and hyperkeratosis. Hair bulbs are atrophic.
- Kidneys: Hyalinazitaion of the glomeruli and fatty degeneration of convulated tubules have been observed.

Pathology 5.

- Hormonal changes: represent an adaptation to nutritional stress. The plasma cortisol concentration is raised with an inrease in growth hormone and the level of insulin is reduced.
- Anaemia: B12 vitamin and folate deficiency, iron deficiency.

Pathology 6.

- Oedema: is constant feature in PEM, mostly due to hypalbuminaemia. Cardiac output is reduced also.
- Carbohydrate metabolism: hypoglycaemia is frequently observed.
- Protein and amino acid metabolism: serum protein concentration is low.

Nutritional marasmus 1.

- Definition:
  - It is a syndrome of severe protein/calorie malnutrition characterised by growth failure (60% or less of expected weight for age), and very wasted muscles and subcutatneous fat. It is due to a diet that is extremely low in both protein and calories.

Nutritional marasmus 2.

- Symptomatology:
  - Constatnt clinical features:
    - extreme growth retardation
    - severe wasting of both muscle and fat
  - Occasional features:
    - anaemia
    - avitaminosis
    - sligt hair changes
    - signs of different infections
- **The tratment is similar to kwashiorkor**

Malnutrition

Malnutritio

Marasmic child