SKELETAL DYSPLASIA Dr Vasu Pai

Skeletal dysplasia are the result of a defective growth and development of the skeleton. Dysplastic conditions are suspected on the basis of abnormal stature, disproportion, dysmorphism, or deformity.

Diagnosis requires

Simple **measurement of height** and calculation of proportionality [<60 inches: consideration of dysplasia is appropriate]

Dysmorphic features of the face, hands, feet or deformity

A complete physical examination

Radiographs: Extremities and spine, skull, Pelvis, Hand

Genetics: the risk of the recurrence of the condition in the family; Family evaluation.

Dwarf:

Proportional: constitutional or endocrine or malnutrition

Disproportion [Trunk: Extremity]

a. Height

< 42" Diastrophic Dwarfism

< 48" Achondroplasia

52" Hypochondroplasia

b. Trunk-extremity ratio

May have a normal trunk and short limbs (achondroplasia),

Short trunk and limbs of normal length (e.g., spondylo-epiphyseal dysplasia tarda)

Long trunk and long limbs (e.g., Marfan's syndrome).

c. Limb-segment ratio

Normal: Radius-Humerus ratio 75%
Tibia-Femur 82%

Rhizomelia [short proximal segments as in Achondroplastics]
Mesomelia: Dynschondrosteosis]
Acromelia [short hands and feet]

RUBIN CLASSIFICATION

Table 2 Rubin Classification

Epiphysis	Hyperplasia	Trevor's disease
	Hypoplasia	SED, MED, pseudoachondroplasia
Physis	Hyperplasia	Enchondromatosis
	Hypoplasia	Achondroplasia, metaphyseal chor
Metaphysis	Hyperplasia	Multiple exostosis
	Hypoplasia	Osteopetrosis
Diaphysis	Hyperplasia	Diaphyseal dysplasia
	Hypoplasia	Osteogenesis imperfecta

1. **Hypoplastic epiphysis ACHONDROPLASTIC**

Autosomal Dominant: 80%; 0.5-1.5/10000 births

Most common disproportionate dwarfism.

Prenatal diagnosis: 18 weeks by measuring femoral and humeral lengths.

Abnormal endochondral bone formation: zone of hypertrophy.

Gene defect FGFR fibroblast growth factor receptor 3 . chromosome 4

Rhizomelic pattern, with the humerus and femur affected more than the distal extremities;

Facies:

Frontal bossing; Macrocephaly; Saddle nose

Maxillary hypoplasia, Mandibular prognathism

Spine: Lumbar lordosis and Thoracolumbar kyphosis

Progressive genu varum and coxa valga

Wedge shaped gaps between 3rd and 4th fingers (trident hands)

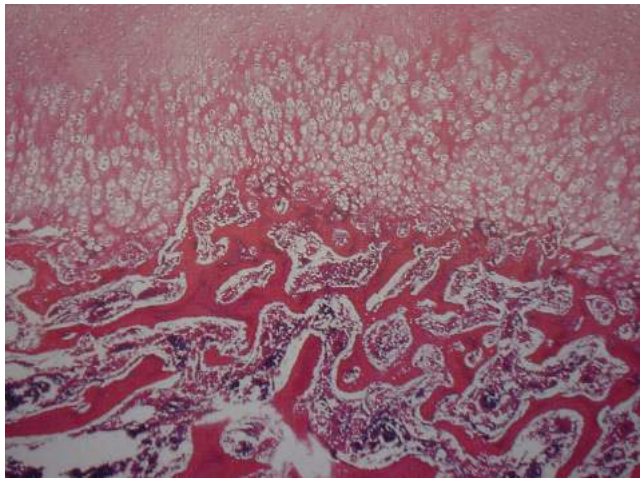
Trident hand 50%, joint laxity

Pathology

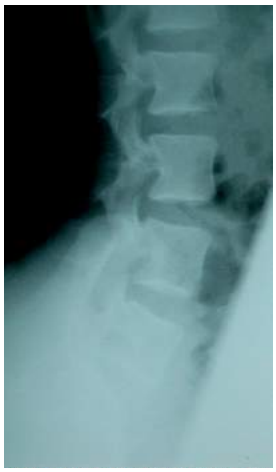
Lack of columnation

Bony plate from lack of growth

Disorganized metaphysis



Orthopaedics



1. Joint laxity syndrome
2. At 1 year: Stenosis of foramena Magnum
3. Severe Thoracolumbar kyphosis in 50%.
   >60° may need Surgery
   T12, L1 wedging with anteroinferior beak.
   Generalised posterior vertebral scalloping.
4. Congenital Lumbar Canal Stenosis 20%
   Decrease interpedicular distance
   excessive lordosis;
   Posterior scalloping of vertebra
5. Pelvis elephant ears, Flat acetabular roof,

   Coxa Valgum Genu varum
6. Elephant years, flat acetabular floor

Treatment

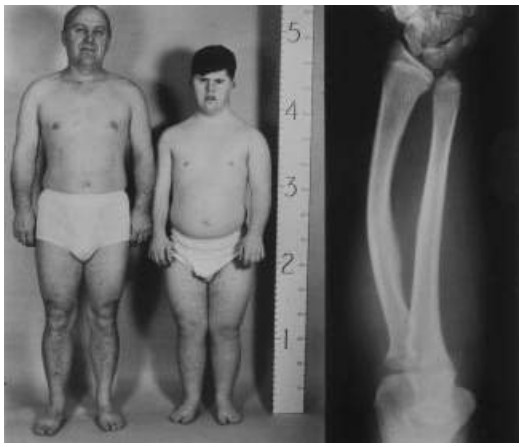
1. Human growth hormone: Effective over first year. ?PTH
2. Bony elongation: Leg lengthening [Ilizarov]

Spine related problems

LCS	Decompression
Kyphosis:	TLSO +/-Anterior and posterior fusion without instrumentation

Hypochondroplasia is typically not diagnosed until the middle or late period of childhood. Disproportionate short limbs. The condition is distinguished from achondroplasia by mild radiographic findings, normal facies, and an adult height taller than that seen in achondroplasia [>52"].

DYSCHONDROSTEOSIS



Mild short stature
Mesomelic limb shortening [short forearm]

Short forearm bones, exaggerated radial bowing, volar angulation of the distal radial epiphyses, and instability of the distal radioulnar articulation (Madelung's deformity).
Transmitted by autosomal-dominant inheritance.

Most common mesomelic dysplasia.

Physis Hyper: MULTIPLE ENCHONDROMA

Figure 1a

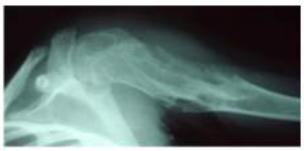
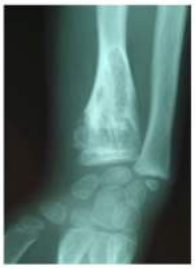


Figure 1b



Usually asymptomatic cartilage tumors, in the diaphysis of long tubular bones, in close proximity to growth plate cartilage.

Enchondromatosis or Ollier disease
presence multiple enchondromas and characterized by an asymmetric distribution of cartilage lesions that can be extremely variable in terms of size, number, location, evolution of enchondromas,

The condition in which multiple enchondromatosis is associated with soft tissue hemangiomas is known as Maffucci syndrome [high rate of Abdominal Carcinoma Phleboliths

.

X ray: The lesions and long bone axis run parallel. The lesions usually calcify with time and become diffusely punctated or stippled, a light trabeculation may be visible. Enchondromas are frequently assembled as clusters, thus resulting in the metaphyseal widening.

The reported incidence of malignant transformation is variable and estimated to occur in 5–50% of the cases. It is higher in Maffucci's syndrome, the prognosis of which is more severe than that of Ollier disease

II Hypoplastic epiphysis MULTIPLE EPIPHYSEAL DYSPLASIA

Multiple epiphyseal dysplasia is relatively common.

Mild short stature; Normal facies.

Varus or valgus knee deformity is common.

The radiographic appearance is normal at birth.

The proximal femoral and other epiphyses are delayed in appearance and are small.

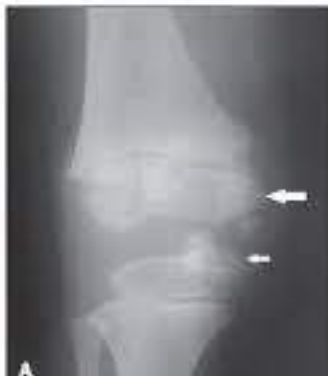
Epiphyseal abnormalities are general and symmetrical and include the spine in adolescence.

Transmitted by autosomal- dominant inheritance.

Young adults often develop severe osteoarthritis of weight-bearing joints.

symmetric involvement of the epiphyses with a delay in their ossification. D/D Perthe's

II Hyperplastic epiphysis Trevor's Dysplasia



Hemimelic epiphyseal dysplasia

Characterized by asymmetric overgrowth of cartilage in the epiphyses.

Histologically, it is an epiphysis osteochondroma.
The symptom onset occurs primarily during childhood.
Males are 3 times more affected than females.

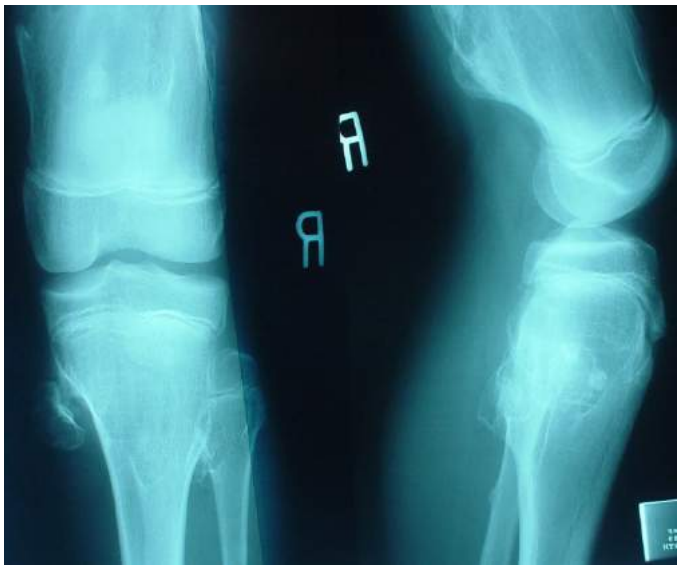
The most common symptom is a painless bony mass around the ankle or knee, followed by swelling, restricted range of motion and deformity.

III Hyperplastic Metaphysis MULTIPLE EXOSTOSIS.

A mutation in the gene coding for **cartilage oligomeric matrix protein**. [COMP] on Chromosome 19

Multiple Exostosis Diaphyseal achlasis

Multiple Exostosis



Common 1:18,000.

At birth normal; Normal facies

The adult height of those affected is about 2 inches shorter

Autosomal Dominant: Deletion of exon 8 from the EXT1 gene

Cause: Remodeling defect

Sessile or pedunculated exostosis

LLD and deformity [Varus or valgus]

Radial club hand

Malignancy usually 1%

III Hypoplastic Metaphysis, OSTEOPETROSIS

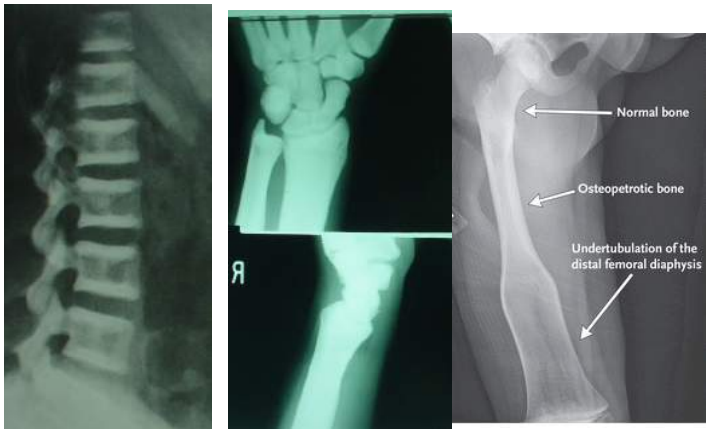
Syn: Marble bone" disease, Albers-Schonberg disease, osteosclerosis

Autosomal Dominant is mild

Autosomal recessive is Malignant [Obliteration of the marrow spaces ➔ anaemia + extramedullary haematopoiesis and hepatosplenomegaly. Hypersplenism]

Osteoclastic activity is inhibited

No remodeling in the metaphysis



Generalised dense bone [loss of medullary cavity]
Jersy spine
Erlenmyer Flask

Treatment Bone marrow transplant

IV Diaphysis

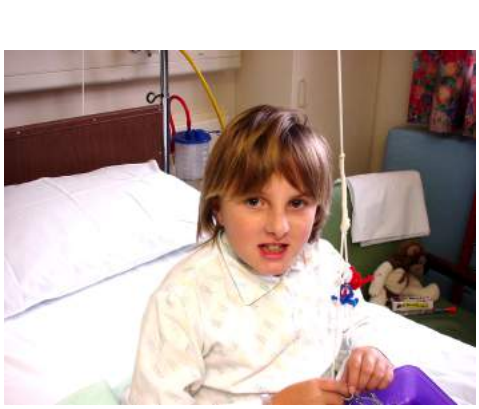
OSTEOGENESIS IMPERFECTA

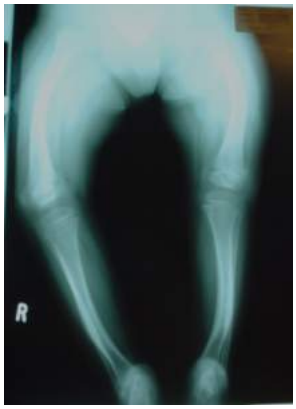
Genes coding for
Mutation in chromosome 17 Alpha1 and
Chromosome 7 for Alpha2

Type I 1: 30,000
Type II 1:60,000; AD [some AR]

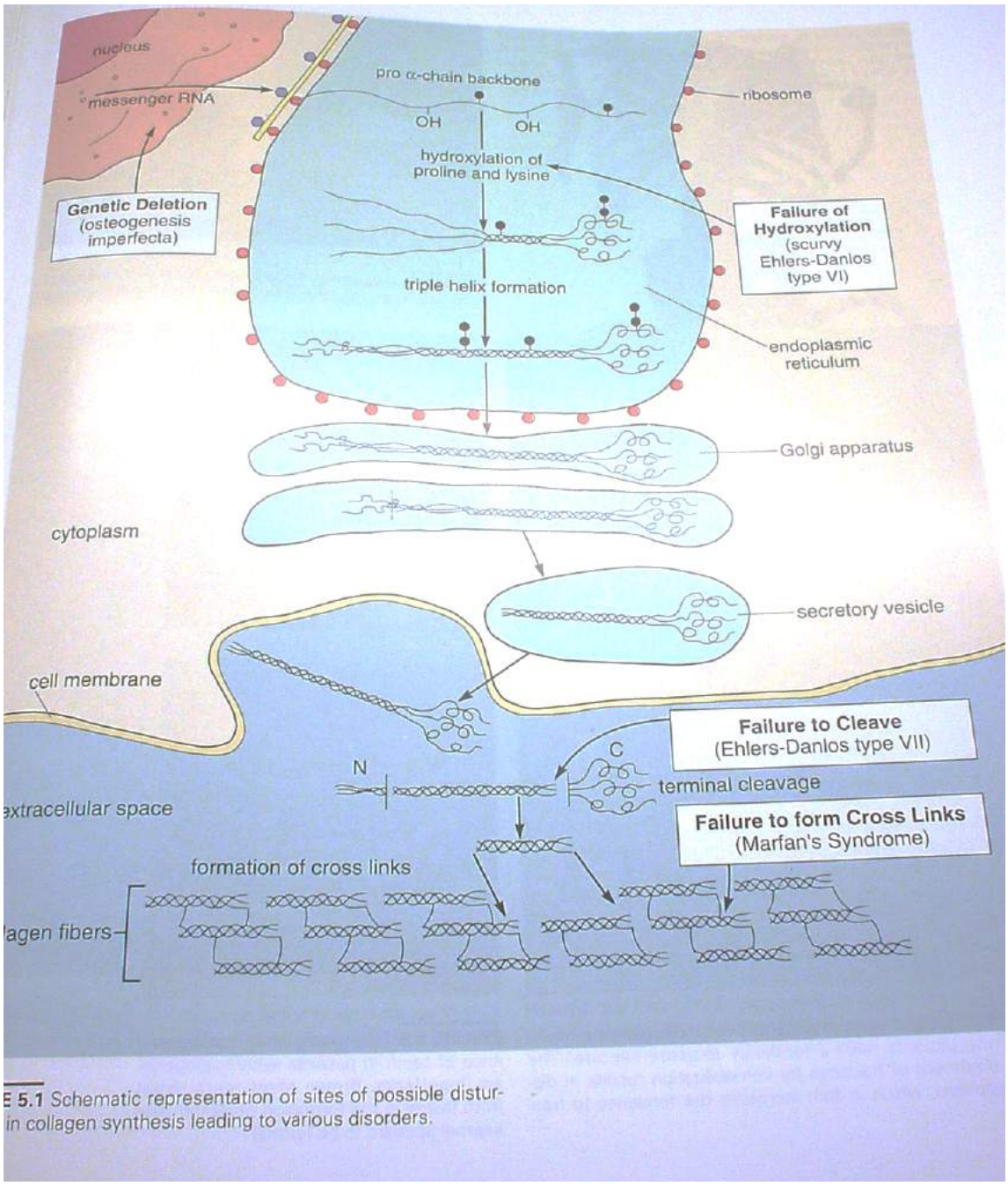
Blue eye, Dental dysgenesis, deafness, neurological defects (macrocephaly and basilar invagination) and cardiopulmonary complications (the major cause of mortality directly related to OI), scoliosis

Brittle bone with deformity of the bone. Healing normal; Remodeling is at fault; More woven bone; wider Haversian canal





Pathogenesis



E 5.1 Schematic representation of sites of possible distur-
in collagen synthesis leading to various disorders.

Sillence Type

	Severity	Growth	Deaf	Sclera	Teeth
I [AD]	Moderate [Tarda]+	+	+	+	+/-
II[AR]	Death	+++	-	+	-
III[AR]	+++	++++	+/ -	-	+/-
IV[Ad]	Moderate	++	-	-	+

(BS= Blue sclera; G = Growth; Deafness = usually conductive deafness)

Histology

Increased diameter of the Haversian canals,

increased numbers of cells

duplication of cement lines.

Pathology

A relative increase in woven bone that does not mature to lamellar bone.

Trabeculae are thin and poorly arranged

Haversian canal system: wide

Bone mineral density is decreased [DEXA]

Fractures heal normally but no remodelling occurs. Fractures less frequent with age

TREATMENT

Villous biopsy; US detect as early as 15 wks in Type II

Skin Biopsy: may require to confirm diagnosis

Regarding medical treatment, intravenous bisphosphonate therapy is the most widely used medical approach.

Gene Therapy:Mutation suppression is modeled on type I OI, in which individuals have a

null allele, make half the normal amount of collagen and have mild disease. Specific suppression of expression of the mutant allele, by hammerhead ribozymes, for example, would transform the recipient biochemically from type II, III or IV OI into type I.

Evaluation of clinical outcome was **complicated by treatment in infancy with bisphosphonate but the child had sustained fractures and had significant growth deficiency**.

Bone marrow transplantation of OI children with marrow-derived mesenchymal cells claimed transient improvement in growth, total body mineral content and fractures, but the methodology of these studies was controversial .

Surgery

1.Telescopic Nail [Bailey-Dubot];

2. Shish Kebab: Multiple osteotomy

3. Scoliosis surgery > 50°

REFERENCES

1. Beals. **J Am Acad Orthop Surg 1995;3:174-18**
2. *Journal of Pediatric Orthopedics. 19(1):122-132,*