MUSCULOSKELETAL BLOCK: LECTURE TWO

CONGENITAL, DEVELOPMENTAL AND METABOLIC BONE DISEASES

DR. AMMAR AL RIKABI

ASSOCIATE PROFESSOR AND CONSULTANT

DEPARTMENT OF PATHOLOGY

KING KHALID UNIVERSITY HOSPITAL

DEVELOPMENT AND GROWTH OF THE SKELETON

During fetal development, bone can be formed either directly in mesenchyme, as in the case of the skull and clavicles (intramembranous ossification) or on pre-existing cartilage (endochondral ossification). In intramembranous ossification, bone is laid down as woven bone that eventually matures into lamellar bone. In endochondral ossification, the cartilaginous template undergoes ossification at particular sites along the bone known as ossification centers. In long bones, the cartilage at the epiphysis persists until after puberty, allowing growth. This area of persisting cartilage is called the growth plate.

Once the bones are fully formed, further growth occurs by the laying down of further bone onto the pre-existing bone. The coordinated actions of the osteoblasts and osteoclasts are paramount in bone development and maintenance. In bone development, the action of osteoblasts predominates. When the skeleton has reached maturity, the bones are continually renewed and remodeled, which requires the actions of the osteoblasts and osteoclasts to be in equilibrium. By the third decade, osteoclastic resorption begins to predominate with a resultant steady decrease in skeletal mass.

DEVELOPMENT DISORDERS

Achondroplasia

Achondroplasia is a major cause of dwarfism and is due to mutation of a single gene. The condition can be familial with autosomal dominant inheritance or sporadic. The defective gene leads to abnormal ossification at the growth plates of bones formed by endochondral ossification. Intramembranous ossification is unaffected. Affected individuals have a characteristic appearance with shortening of the proximal extremities, a relatively normal-sized trunk and a disproportionately large head with typical bridging of the forehead and depression of the nasal bridge.

Osteogenesis imperfect (brittle bone disease)

This is a rare group of genetic disorders that have in common the abnormal synthesis of type I collagen. In addition to bone, the other tissues rich in type I collagen are tendons, ligaments, skin, dentine and sclera. Affected individuals have brittle bone and spontaneous fractures may occur. The sclera appears blue because it is so thin that the underlying uveal pigment becomes visible. Some variants of osteogenesis imperfect are fatal early in life while others are associated with survival.

ACQUIRED DISORDERS

Osteoporosis

Osteoporosis is characterized by reduced bone mass, making bone vulnerable to fracture. Trabecular bone is affected before cortical bone. Trabecular bone is found in the greatest amounts in the vertebral bodies and pelvis and cortical bone is found in the greatest amounts in the long bones.

Aetiology and pathogenesis

Osteoporosis may be primary or secondary. Primary osteoporosis refers to senile osteoporosis and post-menopausal osteoporosis. Secondary osteoporosis is due to conditions other than age or menopause such as reduced mobility (e.g. after fracture or associated with rheumatoid arthritis), smoking and alcohol consumption, endocrine disorders (e.g. Cushing's syndrome, hyperthyroidism, diabetes) and corticosteroid therapy. Obesity and exercise appear to be protective against osteoporosis.

Senile osteoporosis. There is a normal progressive loss of bone mass after around the age of 30 years, and so all elderly people will have some degree of osteoporosis. Bone loss rarely exceeds 1% per year. The

higher the initial bone density, the lower the risk of significant osteoporosis. Women are at higher risk than men, and white people are at higher risk than black people.

Post-menopausal osteoporosis. Post-menopausal osteoporosis is characterized by hormone-dependent acceleration of bone loss. Post-menopausal women may loose up to 2% of cortical bone per year and up to 9% of trabecular bone per year for 8-10 years associated with declining to the normal rate of bone loss after that. Estrogen deficiency is thought to have a major role and estrogen replacement at the beginning of the menopausal reduces the rate of bone loss.

Clinical features

The major complication of osteoporosis is bone fracture. The sites most commonly affected are the vertebral bodies, the distal radius (Cole's fracture) and the hips. Fractures of the vertebral bodies can be of the crush variety leading to progressive loss of height and considerable pain **or** of the wedge or triangular shaped type which causes deformity of the spine (kyphosis). Hip fractures are important because they cause major disability and lead to hospital admission. Secondary complications such as pneumonia and pulmonary thromboembolism are common with hip

fractures and account for the high mortality rate associated with hip fractures.

Treatment

Women who take hormone replacement therapy have a reduced risk of developing post-menopausal osteoporosis. Also, oral bisphosphonates and vitamin D may be effective.

METABOLIC BONE DISEASE

Rickets and osteomalacia

Osteomalacia is characterized by defective mineralization of the osteoid matrix and is associated with lack of vitamin D. When the condition occurs in the growing skeleton (children) it is called rickets. Vitamin D is important in the maintenance of adequate serum calcium and phosphorous levels and deficiency impairs normal mineralization of osteoid laid down in the remodeling of bone. The result is osteomalacia. In children, lack of vitamin D leads to inadequate mineralization of the epiphyseal cartilage as well as the osteoid, resulting in rickets.