OSTEOGENESIS IMPERFECTA

What happened to Mr. Glass?
OSTEOGENESIS IMPERFECTA

According to the National Institute of Health, Osteogenesis Imperfecta is a genetic disorder characterized by bones that break easily, often from little or no apparent cause. (NIH). It is generally caused by a hereditary collagen defect. A small percentage of OI sufferers acquired it through a random mutation in the collagen gene. There are eight known types of Osteogenesis Imperfecta (OI). It occurs in all races though the prevalence of a type seems to vary from one geographical location to another. The disease has been known under various names throughout history. The most common ones are Ekman-Lobstein Syndrome, Vrolik Syndrome, and Glass-bone Disease. It acquired the name “Osteogenesis Imperfecta” around the 19th century. Studies suggest that there are currently 20,000 to 50,000 people suffering from OI in the United States. (NIH).

DIAGNOSIS
The general diagnosis is done based the presentation of traits particular to OI. More in depth tests such as the biochemical and molecular genetic test confirm (or may dispel) prior hypothesis and add further information regarding the type of OI present.

Osteogenesis Imperfecta types are classified into two major groups:
- **Dominant or classical OI**
  This group accounts for 85 to 90% of OI cases. It is associated with a mutation due to an improper amino acid substitution of glycine in the collagen’s triple helix structure. (Wikipedia). The hydrolyzation of the improper collagen structure results in low quality collagen production. The percentage of properly formed collagen is thus noticeably reduced. The types I through IV are found under this category
- **Recessive OI**
  This group accounts for 10 to 15% of OI cases. It is associated with mutations in other genes causing interference in the collagen formation process. The types VII and VIII are found under this category.

A third category is for the types V and VI which remain under investigation for proper categorization. In all cases, the bones formed are altered. Besides the general malformations of the long bones in the appendicular skeleton, OI patients are also present scoliosis, craniofacial malformations including larger than normal head, malformed dental arches, teeth, upper and lower jaws, and bulging bitemporal bone.

**Dominant Forms of Osteogenesis Imperfecta**

**Type I**
- most common and mildest type of OI
- normal collagen structure, but less than normal amount
- bones predisposed to fracture (most fractures occur before puberty)
- normal or near-normal stature
- loose joints and muscle weakness
- blue, purple, or gray tint to sclera (whites of the eyes)
- triangular face
- slight spinal curvature
- absent or minimal bone deformity
- possible brittle teeth
• possible hearing loss, often beginning in early twenties or thirties
• slight protrusion of the eyes
• associated with Col1A1 and/or Col1A2 malfunction

Type II
• most severe form of OI
• improperly formed collagen with total production of collagen below normal quantity
• frequently causes death at birth or shortly after, because of respiratory problems or intracerebral hemorrhage
• numerous fractures and severe bone deformity
• small stature with underdeveloped lungs
• blue, purple, or gray tinted sclera
• associated with Col1A1, Col1A2, and CRTAP malfunction

Type III
• referred to as progressive and deforming
• easily fractured bones (fractures often present at birth, and x rays may reveal healed fractures that occurred before birth.)
• improperly formed collagen with normal quantity produced
• small stature
• blue, purple, or gray tinted sclera
• loose joints and poor muscle tone in arms and legs
• barrel-shaped rib cage
• triangular face
• spinal curvature
• possible respiratory problems
• often severe bone deformity
• possible brittle teeth
• possible early hearing loss

Type IV
• between Type I and Type III OI in severity
• improperly formed collagen with normal quantity produced
• bones easily fractured (most fractures occur before puberty)
• smaller than average stature
• sclera normal in color (i.e., white or near-white)
• mild to moderate bone deformity
• spinal curvature
• barrel-shaped rib cage
• triangular face
• possible brittle teeth
• early hearing loss
• mild to moderate bone deformity

Osteogenesis Imperfecta: Unknown Class
Type V

- clinically similar to Type IV OI in appearance and symptoms
- a dense band seen on x-rays adjacent to the growth plate of the long bones
- hypertrophic calluses, at the sites of fractures or surgical procedures
- calcification of the radio-ulnar interosseous membrane, which leads to restriction of forearm rotation
- sclera normal in color (i.e., white or near-white)
- normal teeth
- “mesh-like” appearance to bone when viewed under the microscope
- dominant inheritance pattern
- no mutation in Col1 present

Type VI

- clinically similar to Type IV OI in appearance and symptoms
- slightly elevated activity level of alkaline phosphatase (an enzyme linked to bone formation), which can be determined by a blood test
- distinctive “fish-scale” appearance to bone when viewed under the microscope
- diagnosed by bone biopsy
- unknown whether this form is inherited in a dominant or recessive manner, but researchers believe the mode of inheritance is most likely recessive
- Eight people identified with this type of OI to date

Recessive Forms of Osteogenesis Imperfecta

Type VII

- discovered in 2005
- resembles Type IV OI in many aspects of appearance and symptoms in the first described cases
- in other instances, similar appearance and symptoms to Type II lethal OI, except infants had white sclera, a small head, and a round face
- small stature
- short humerus and short femur
- coxa vara is common (deformed hip joint in which the neck of the femur is bent downward); the acutely angled femur head affects the hip socket.
- results from recessive inheritance of a mutation in the CRTAP gene. Partial (10%) expression of CRTAP leads to moderate bone dysplasia. Total absence of the cartilage-associated protein has been lethal in all identified cases. This type found mainly in Quebec (Canada).

Type VIII

- resembles lethal Type II or Type III OI in appearance and symptoms, except infants have white sclera
- severe growth deficiency
- extreme skeletal undermineralization
- caused by absence or severe deficiency of prolyl 3-hydroxylase activity due to mutations in the LEPRE1 gene

TREATMENT

No cure has been developed to date for OI. Various treatments options are being researched in order to afford OI sufferers as close to a normal life as possible by strengthening their bones and muscles to
increase their ability to safely and freely move and reduce the risk of fatal fractures. Mobility aids such as wheelchairs, crutches, splints, grabbing arms, and braces are often used to assist OI sufferers in achieving some level of autonomy. The corrective options in use are:

1. **PHYSIOTHERAPIES**
   This therapy form is considered the gentlest non-chemical treatment form. It encompasses targeted physical therapy and water therapy. Support cushions (including sole inserts in shoes, cushions at the base of the spine and/or in the lumbar region) are used for balance and scoliosis correction. Therapeutic exercises such as swimming and walking, and periodical shifts in body position are recommended.

2. **CHEMICAL THERAPIES**
   Drugs, gene and growth hormone therapies are being explored to relieve the symptoms of OI. Teriparatide is a synthetic form of the parathyroid hormone given adult OI patients to regulate bone metabolism. Alendronate is a bisphosphonate given preteen OI patients to increase bone mass by slowing the effects of osteoclasts while promoting that of normal osteoblasts. Bisphosphonate therapy (oral or intravenous) is growing in popularity in the USA and the growing popularity is inspiring an increasing number of clinical trials in order to better assess the associated long term advantages and disadvantages.

3. **SURGERY**
   This therapy form is more invasive and includes procedures such as rodding and spinal fusion. Rodding involves inserting a stainless steel rod in the intramedullary canals of the long bones to strengthen them and prevent or correct deformities. Spinal fusion is performed to correct scoliosis causing pressure on the brain stem and spinal cord.

**CONCLUSION**
Osteogenesis Imperfecta sufferers are advised to keep from smoking, consuming steroids, too much alcohol and caffeine, which could further weaken their bones. Though they suffer many fractures and have to restrict their activities, both children and adults are able to live as viable members of society. A few examples are the American actor Michael J. Anderson, the British actress Julie Fernandez, the American Olympic bronze medalist Doug Herland.
ATTACHMENTS

Figure 1 - Blue sclera as present in OI

Figure 2 - Radio imaging of effects of OI on bones
REFERENCES