Amelogenesis Imperfecta (AI)

Classification, characteristics and management

Dr Jilen Patel

Definitions

- AI “implies a generalized fault of enamel structure affecting all the teeth of one or both dentitions. The faults do not seem to be related to any specific period of time during enamel development, nor to any intercurrent disease or dietary abnormality. It may be hereditary or may occur spontaneously in one or more members of a family”

  (Darling 1956)

- “all the individuals in the kindred show essentially the same defect and which are unassociated with known morphologic or biochemical changes elsewhere in the body”

  (Rao et al 1971)

Definitions

- one gene, one condition?
- “A group of conditions, genomic in origin, which affect the structure and clinical appearance of enamel of all or nearly all the teeth, and which may be associated with morphologic or biochemical changes elsewhere in the body”

  (Aldred et al 2003)
- AI a feature of various syndromes including Morquio, trichodento-osseus, Kohlschütter and, oculo-dento-osseous dysplasia, tuberous sclerosis and vitamin D-dependent rickets

  (Pindborg 1982)

Classification

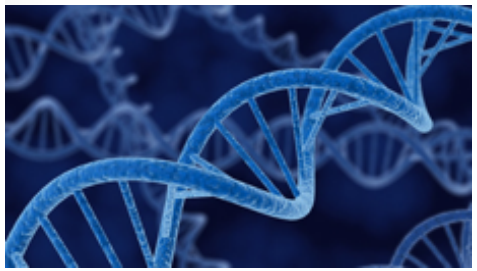
History

- first reported by Spokes in 1890 who described the condition as "hereditary brown teeth”
- distinction between hereditary defects confined to enamel ie AI and those confined to dentine

(Finn 1938)

- AI could be classified into two types: hypoplastic and hypocalcified

(Weinmann et al 1945)



Classification

- based on phenotype and mode of inheritance…useful for clinicians

problems?

- variability in the phenotypic expression
- genotypic information should be used to distinguish between forms of AI
- patients want information about their condition that relates not only to themselves but also to their families

(Aldred et al 2003)

Classification

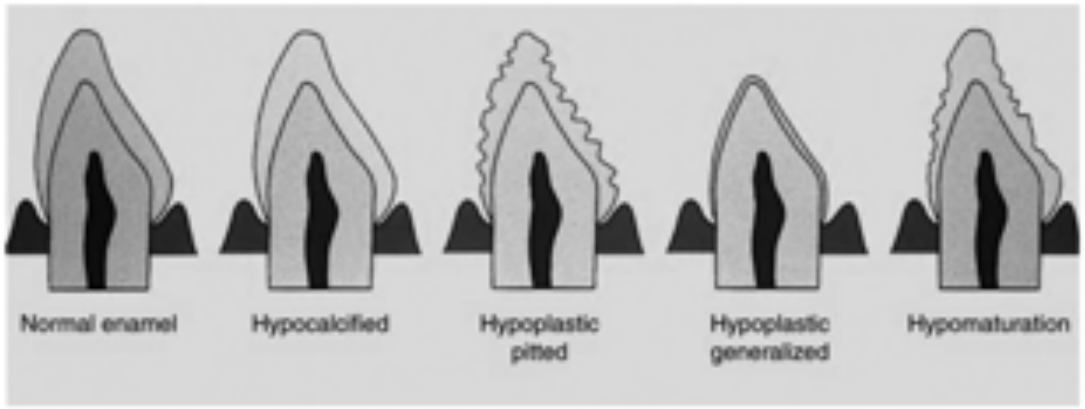


Figure 1. Amelogenesis imperfecta. Diagram of enamel defects of basic types. Hypocalcified - normal thickness, smooth surface, less hardness. Hypoplastic, pitted - normal thickness, pitted surface, normal hardness. Hypoplastic, generalized - reduced thickness, smooth surface, normal hardness. Hypomaturation - normal thickness, chipped surface, less hardness, opaque white coloration.

This figure was published in Contemporary Oral and Maxillofacial Pathology, Sapp J, Eversole L, Wysocki G; Developmental Disturbances of the Oral Region, page 19; Mosby, Inc. 2004.[18]

Prevalence

- 56,663 children from Northern Sweden the prevalence of AI was found to be 1:714

  (Bäckman 1986)
- 96,471 children from the state of Michigan, USA reported a prevalence of 1: 14,000

  (Witkop Jr 1958)
- hypoplastic (60 – 73%), hypomaturation (20 – 40%) and hypocalcification (7%)

  (Chaudhary *et al* 2009; Kwok-Tung *et al* 2007)

Aetiology

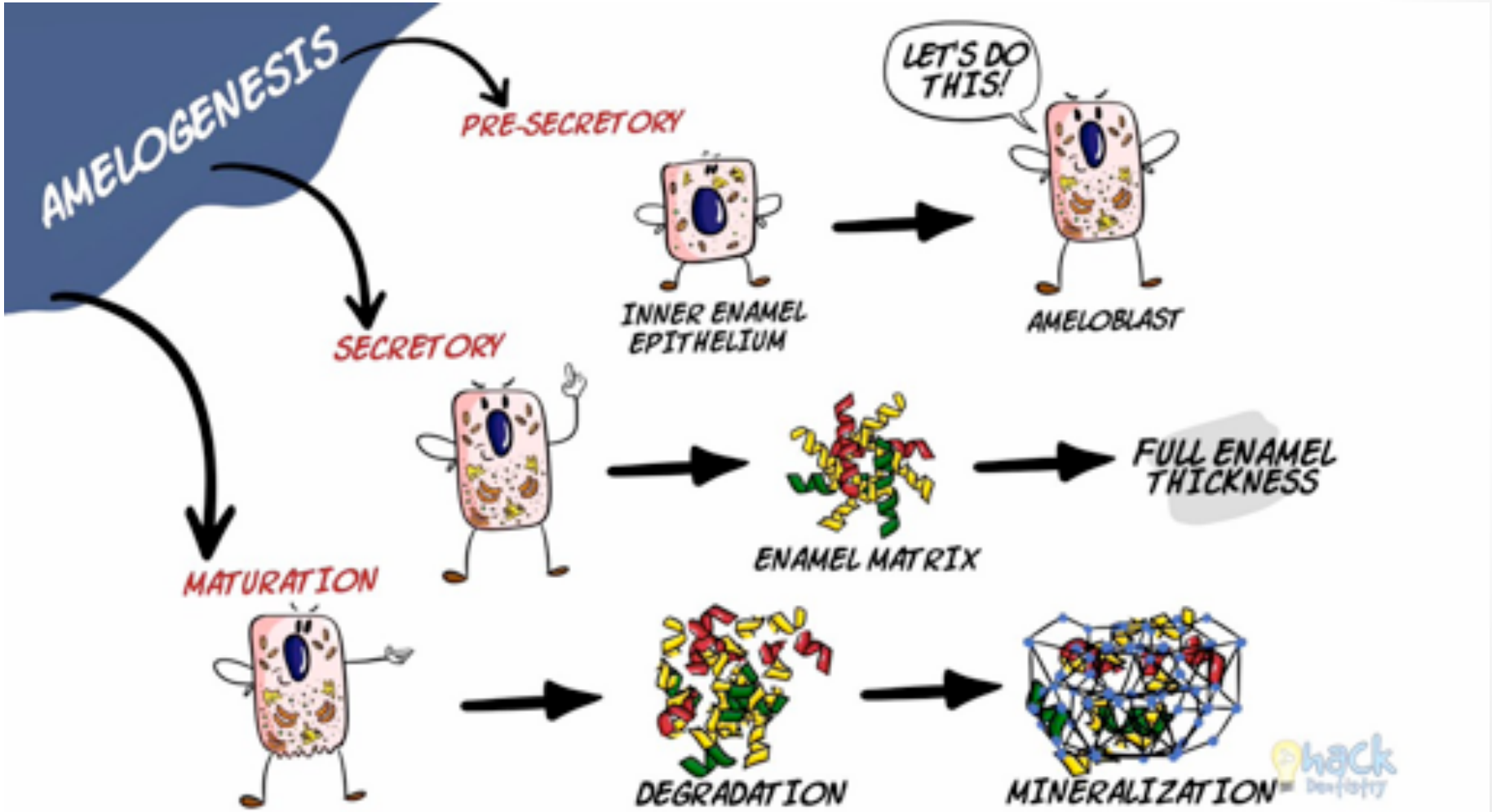
organic matrix molecules:

- enamelin (*ENAM*; 4q21, OMIM *606585)
- amelogenin (*AMELX*; Xp22.3-p22.1, OMIM *300391)
- ameloblastin (*AMBN*; 4q21, OMIM *601259)
- tuftelin (*TUFT1*; 1q21, OMIM *600087)
- amelotin (*AMELOTIN* 4q13) [14]
- dentine sialophosphoprotein (*DSPP*; 4q21.3, OMIM *125485)

enzymes:

- kallikrein 4 (*KLK4*; 19q13.3–q13.4, OMIM *603767)
- matrix metalloproteinase 20 (*MMP20*; 11q22.3–q23, OMIM *604629)

Amelogenesis



Amelogenesis

- **Secretory stage**: a proteinaceous extracellular matrix is incrementally laid-down by epithelially-derived ameloblasts via specialised cellular extensions termed Tomes' processes.

- This matrix partially mineralises to delineate the enamel architecture which is characterised by bundles of enamel crystals (enamel prisms or rods) interdigited with interprismatic enamel crystals

- As the enamel layer approaches full thickness, the Tomes' process is retracted and the final outer enamel layer is aprismatic.

Amelogenesis

- The ameloblasts then enter the **transition stage**, characterised by reduced matrix protein secretion and internal reorganization

- The cells then enter the **maturation stage** and begin secreting the serine protease KLK4 that completely degrades the proteinaceous matrix, leaving the immature enamel crystals bathed in enamel tissue fluid.

Amelogenesis

- The significant increase in the active transport of mineral ions into the matrix during this stage accelerates enamel crystal growth in both width and thickness until the tissue volume is eventually occluded by mineral.

- Finally, the ameloblasts reduce, undergo apoptosis and on tooth eruption, are completely lost

Amelogenesis Imperfecta

- hypoplastic (60 – 73%),
- hypomaturation (20 – 40%)
- hypocalcification (7%)

(Chaudhary *et al* 2009; Kwok-Tung *et al* 2007)

Characteristics

- Hypoplastic form (Bäckman 1989)



- enamel does not reach normal thickness during development
- thin enamel, loss of mesiodistal contact, enamel pits or vertical or horizontal fissures in the enamel

Characteristics

- Hypomaturation form (Bäckman 1989)



- mottled brown-yellow-white appearance, enamel is generally of normal thickness and teeth meet at contact points
- female carriers may have vertical stripes of opaque white enamel alternating with bands of normal enamel (due to Lyonisation)

Characteristics

- Hypocalcified form (Bäckman 1989)



- enamel tends to be so soft that it may be lost soon after eruption, leaving a crown composed only of dentin
- radiographically the enamel fails to contrast with the dentin

Characteristics

Table 1: Witkop classification of amelogenesis imperfecta

Characteristics of four main amelogenesis imperfecta types

Type	*Clinical appearance*	*Radiographic appearance*	*Inheritance*
Hypoplastic (type I)	Multiple enamel pits, severe attrition of the enamel leads to opening of the proximal contact area, snow-capped appearance, thin enamel layer with yellow or brown color, permanent teeth eruption problems	The enamel contracts well with the dentin	AD, AR X-linked D
Hypomaturation (type II)	The enamel is mottled in appearance, relatively normal in thickness, but it is softer than normal, the teeth appear as creamy opaque to yellow brown, often with open bite and dental sensitivity. Hypomineralization is often manifested as enamel chipping or wearing	Radiodensity of the enamel is similar to the dentin	AD, AR X-linked D
Hypocalcified (type III)	The teeth is opaque white or yellowish brown, the enamel surface is rough, the enamel has a normal thickness, the enamel chips away easily, and there are dental sensitivity, open bite, heavy calculus formation	Enamel has contrast similar to or less than dentin, unerupted crowns have normal morphology	AD, AR
Hypomaturation/ hypoplasia/ taurodontism (type IV)	Similar to both the hypoplastic and hypomature types, in addition to taurodontism and anterior open bite with skeletal basis	Enamel contrast normal to slightly more than dentin, large pulp chambers	AD

chambers and has been associated with a mutation within the human DLX3 gene

(Dong et al 2005)


a


b


C


d


e


f


g


h

Diagnostic challenges

Condition	Characteristics
Amelogenesis Imperfecta	Involves all teeth, family history usually present, assosciated anomalies based on type: AOB, taurodontism
Fluorosis	diffuse opacities, usually not associated with caries, number of teeth involved depends on time of exposure, environmental history
Molar incisor hypomineralisation	well demarcated opacities, involves FPMs +/- incisors only, can be associated with PEB and secondary caries
Chronological hypoplasia	number of teeth involved and extent of hypoplastic defects depends on time of disruption, no genetic involvement. Symmetrical, chronological pattern, linear, ring-like pattern

Diagnostic challenges



Chronological hypoplasia

Diagnostic challenges



Chronological hypoplasia

	Calcification begins at
Central incisiors	3-4 mo
Lateral incisors	Maxilla: 10-12 mo Mandible: 3-4 mo
Canines	4-5 mo
First premolars	18-24 mo
Second premolars	24-30 mo
First molars	Birth
Second molars	30-36 mo
Third molars	Maxilla: 7-9 y Mandible: 8-10 y

Ultrastructural Characteristics

- histological sections of hypoplastic AI: pitted, rough with irregular cracked borders
- SEM analysis: irregular and disorganised superficial enamel layer

  (Gopinath *et al* 2004)
- presence of external defects, incorrectly oriented enamel prisms and enlarged interprism spaces

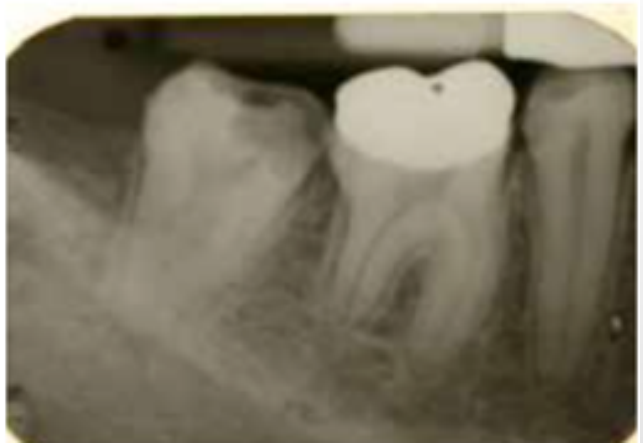
  (Belcheva *et al* 2016)
- reduced tooth mineral density

Associations

intracoronal resorption

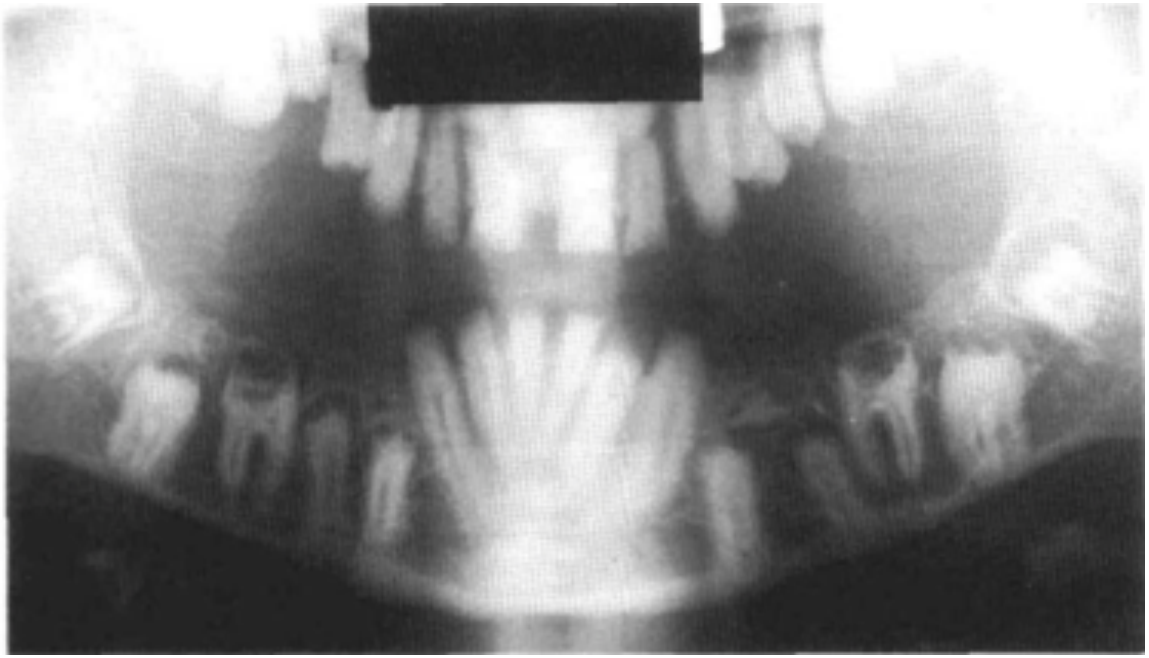
- aggressive, asymptomatic and is often diagnosed incidentally from radiographs
- secondary caries
- pathogenesis unknown
- contributing factors
  - include ectopic positioning of affected teeth,
  - periapical inflammation of a primary precursor
  - developmental defect due to inclusion of uncalcified enamel matrix

(Bhatia *et al* 2015)



Associations

- failure of eruption
- reported in several case reports
- factors: concurrent follicular enlargements, abnormality in the molecular control of the eruption process, space deficiency and the dental alignment problems



(Williams *et al* 1988)

Nephrocalcinosis syndrome

- first reported in 1972

  (MacGibbon 1972)
- case reports reporting failure of eruption, enamel agenesis, unexplained nephrocalcinosis, and normal biochemical parameters
- role of paediatric dentists in early referral of patients with AI to exclude renal pathology

  (Hunter *et al* 2007)

Management

- early diagnosis
- clinical problems include
  - esthetics
  - dental sensitivity
  - loss of occlusal vertical dimension due to loss of dental structure
  - dental caries and/or gingival inflammation
  - orthodontic considerations
  - eruption abnormalities

  (Seow 1992, Gibbard 1974)
- primary aim in the management of AI is to ensure a pain-free, aesthetic and efficient masticatory apparatus for the patient

  (Gibbard 1974)

Management primary dentition











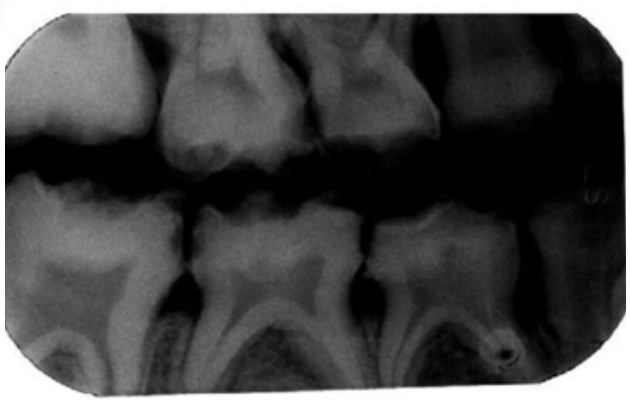
Marquezin et al 2015

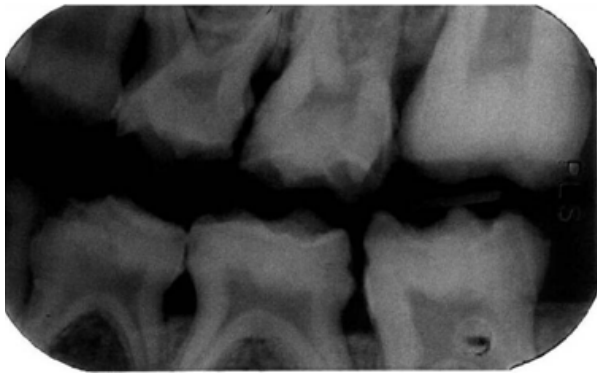
Management mixed dentition



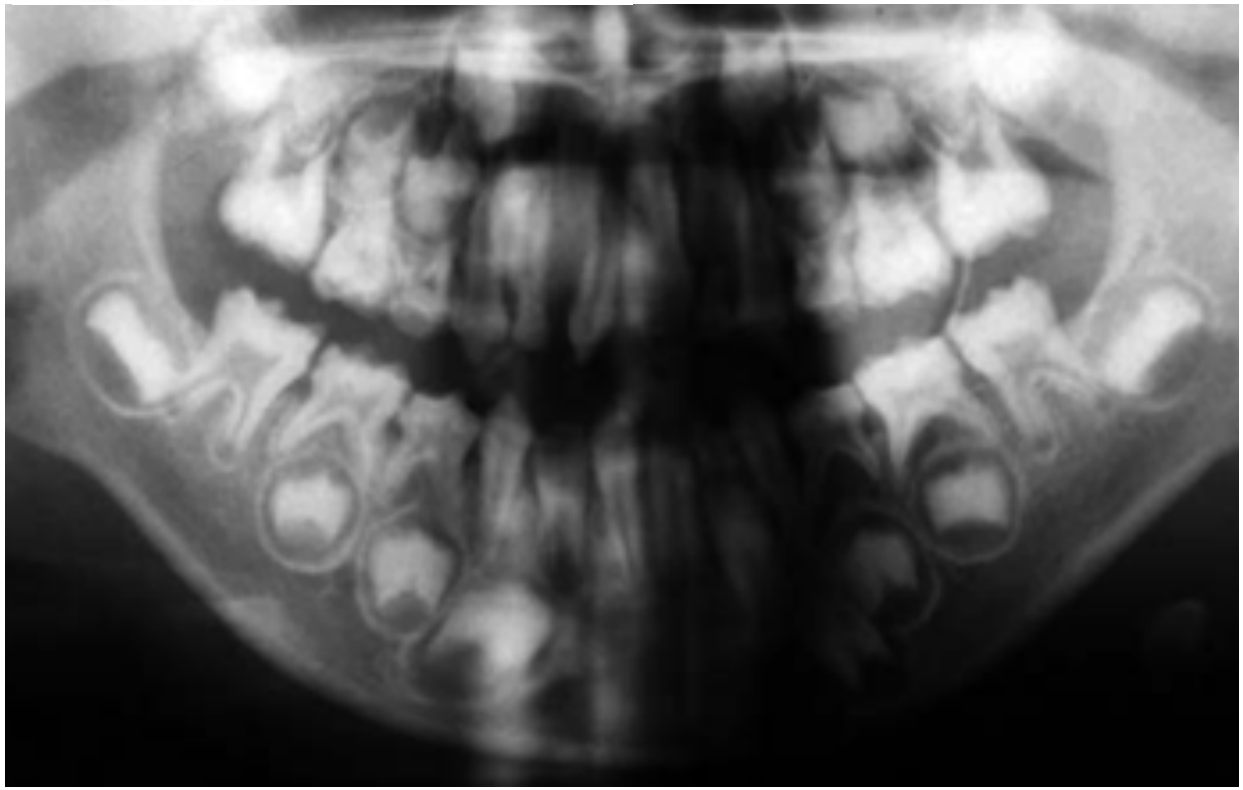
(Kwok-Tung and King 2006)

Management mixed dentition





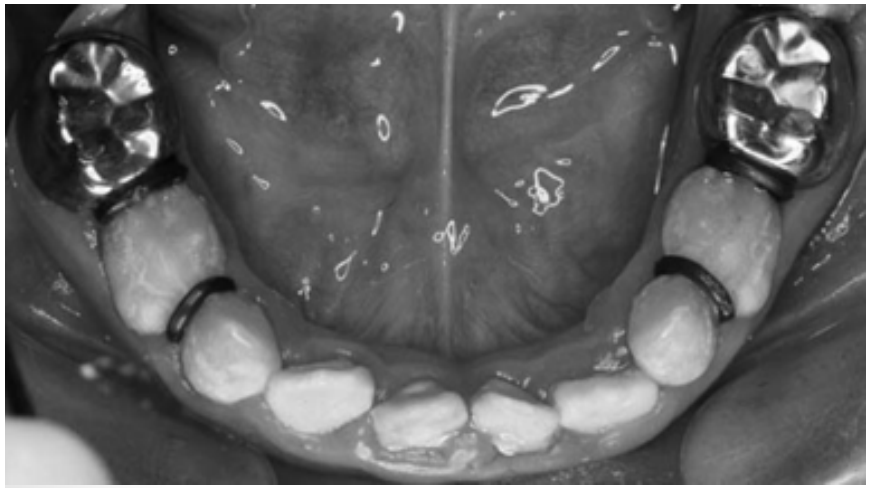


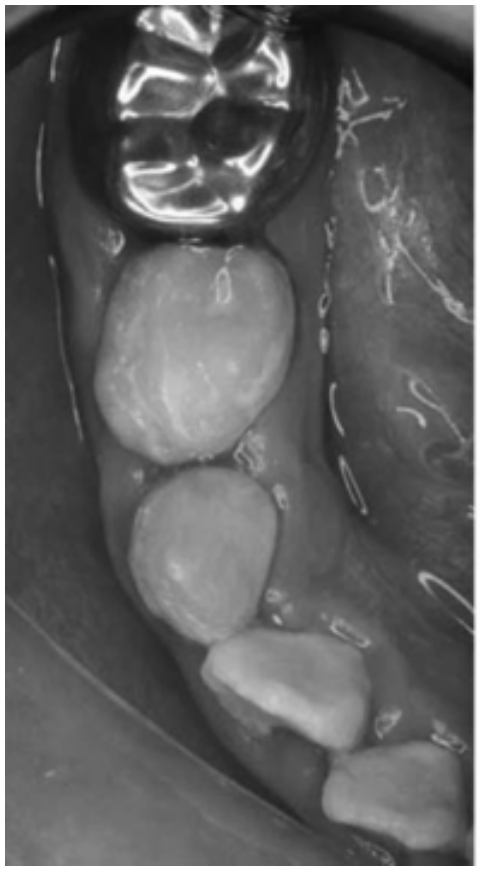


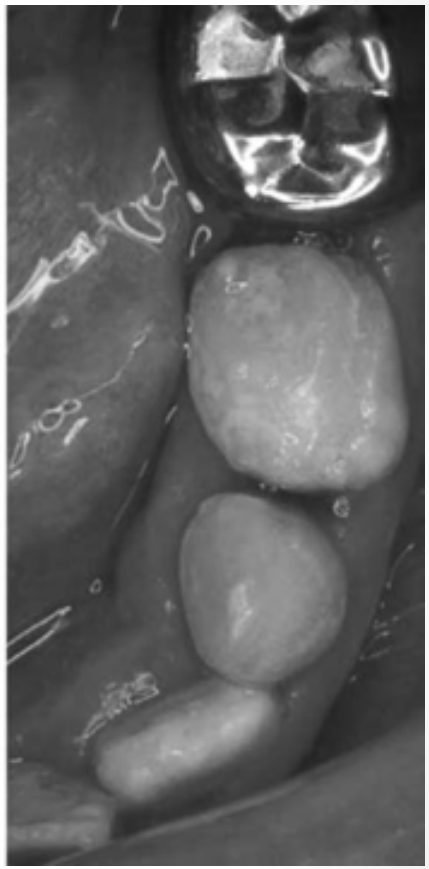
(Kwok-Tung and King 2006)

Management mixed dentition





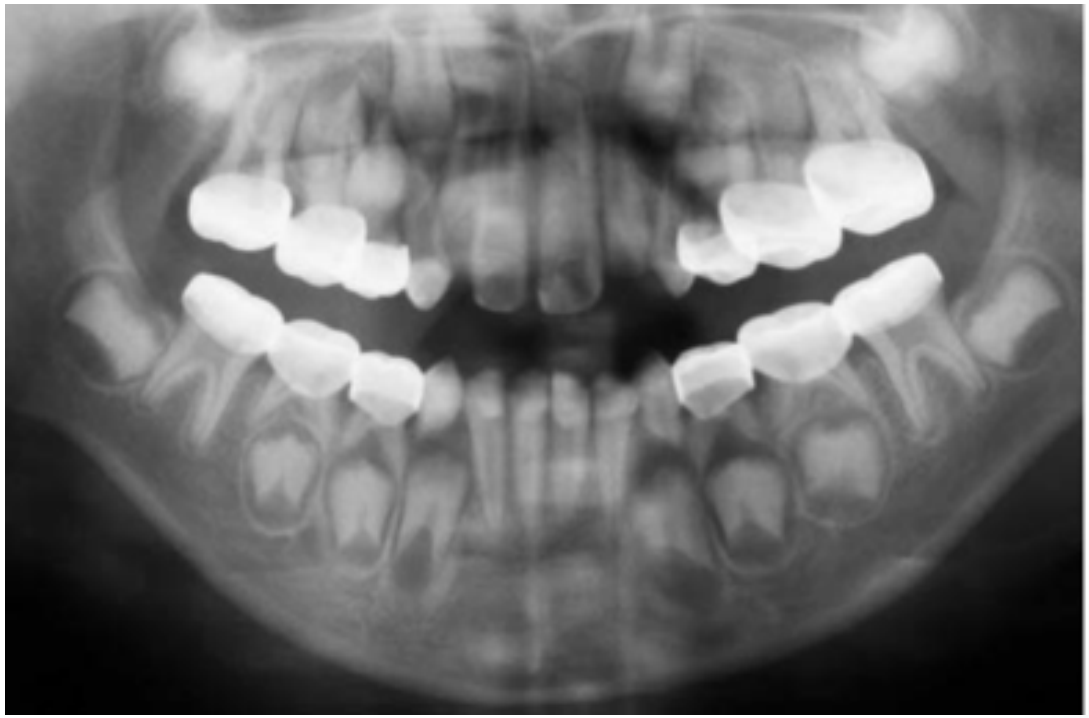




(Kwok-Tung and King 2006)

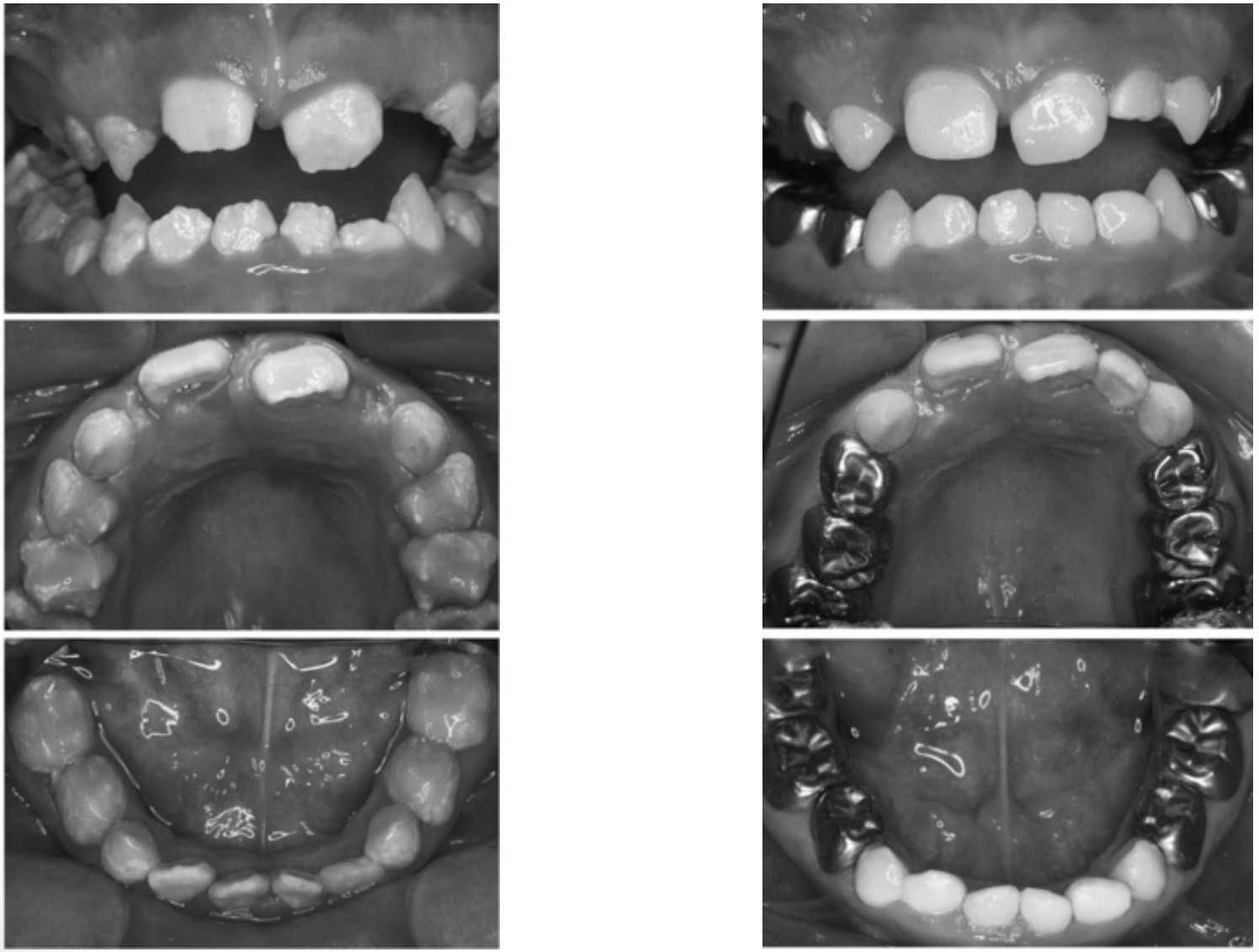
Management mixed dentition





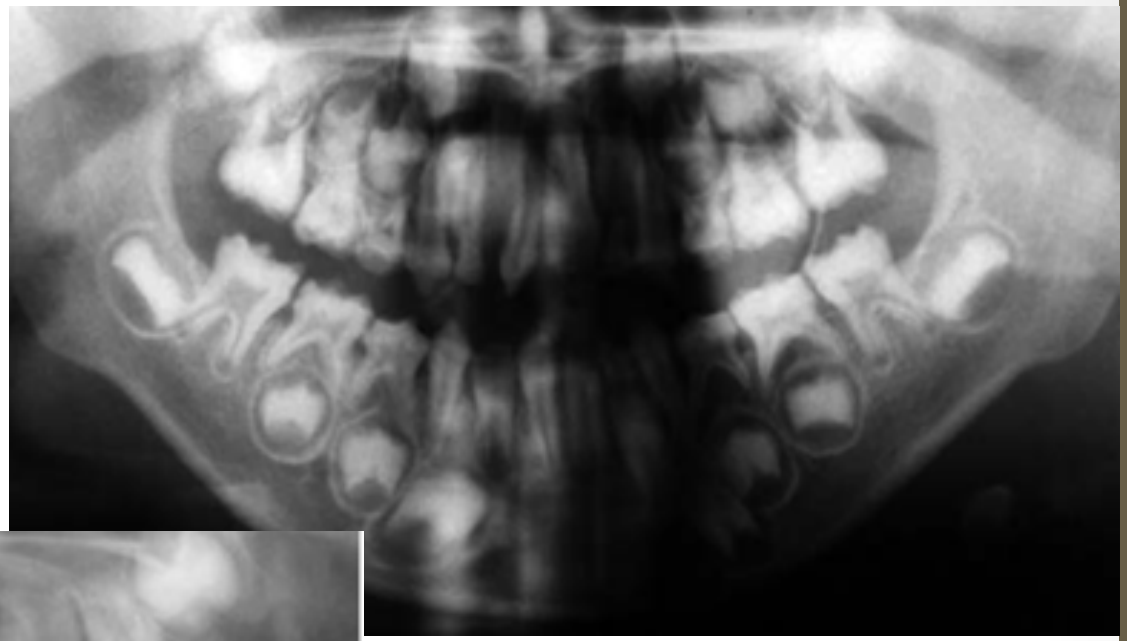
(Kwok-Tung and King 2006)

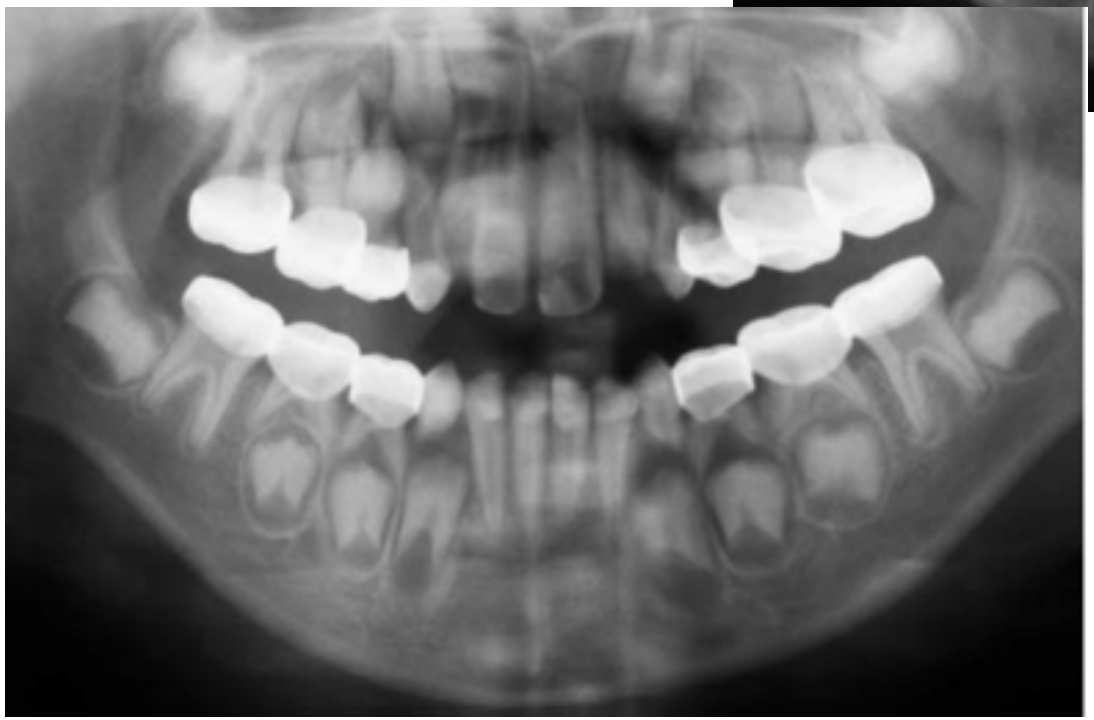
Management mixed dentition



(Kwok-Tung and King 2006)

Management mixed dentition





(Kwok-Tung and King 2006)

Management permanent dentition



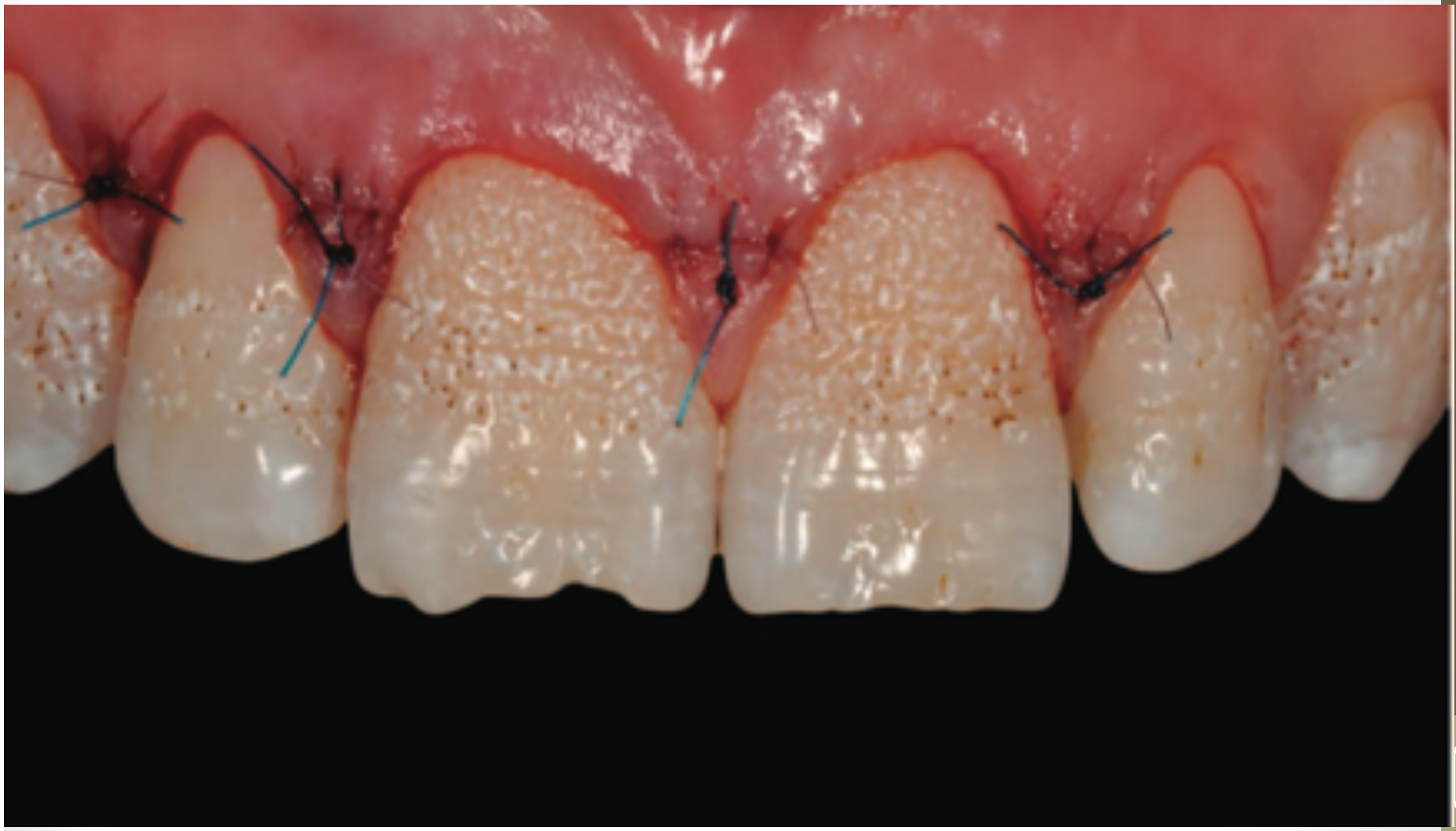
(Shibata et al. 2016)

Management permanent dentition



(Shibata et al. 2016)

Management permanent dentition



(Shibata et al. 2016)

Management permanent dentition



(Shibata et al. 2016)

Management permanent dentition



(Shibata et al. 2016)

Management permanent dentition



(Shibata et al. 2016)

Conclusion

- AI is a rare condition and a number of classifications have been proposed over the years corresponding to advancements made in genetic testing and molecular biology
- the genomic origin of AI gives rise to a number of phenotypic characteristics and identifying the different variants of AI can be particularly challenging
- AI presents a number of clinical challenges including esthetics, attrition, dental sensitivity and orthodontic complications.
- management is focused on prevention, genetic counseling, early diagnosis and management.