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原文作者姓名：	Garg A, Utreja A, Singh SP, Angurana SK
通訊作者學校：	Unit of Orthodontics & Department of Pediatrics Oral Health Sciences Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India.
報告者姓名(組別)：	林慧能 Intern H 組
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內文：

Abstract:

1. Neural tube defects are common congenital malformations at birth or in later stages of life.
2. Morbidity is high in anencephaly, or neurological and motor disorders in spina bifida.
3. Common problems in clinical dentistry:
   Latex allergy, dental caries, difficulty in mouth opening, difficulty sitting in a dental chair, and a high risk of anaphylactic response during anaesthesia.
4. Associated craniosynostosis causing maxillary deficiency, and malformed sella turcica
5. Association of defects has been linked with orofacial clefts and Down syndrome.

Introduction:

- **Neural tube defects (NTD)** are malformations secondary to abnormal neural tube closure. They manifest between the third and fourth weeks of gestational age, resulting in structural defects that occur anywhere along the neural axis from the developing brain to the sacrum.

Methodology:

- Medline database, PubMed, Google (published between 1975 and 2011), and systematic reviews from Cochrane database and websites of international dental organizations

Etiology and pathogenesis:

- Hyperhomocysteinemia due to deficiency of vitamins B6, B11 and B12
- Infants with mutations in the folate receptor-a gene
- Genes of Methylenetetrahydrofolate reductase (MTHFR)
- Low socioeconomic status, smoking, excess vitamin A, zinc deficiency, and high levels of organic
- Maternal obesity, diabetes, the common cold in the first trimester, hyperthyroidism, stress, hyperthermia, and infections.
- Use of antiepileptic drugs during pregnancy causing free-radical induced damage.

Theories of neural tube closure:

- Neural tube defects can be classified by closure sites where failure of closure occurs.
  - Five sites of initiation of neural fold fusion (Van Allen model)
  - Three sites of initiation of neural fold fusion
  - Two sites of initiation of neural fold fusion

Classification of NTD:

- Based on embryological considerations and the presence or absence of exposed neural tissue
  - Open NTD
    - ✓ Due to failure of primary neurulation

✓ Brain and/or spinal cord are exposed at birth through a defect in the skull or vertebrae

✓ Associated cerebrospinal fluid leakage (e.g. spina bifida, anencephaly, and encephalocele).

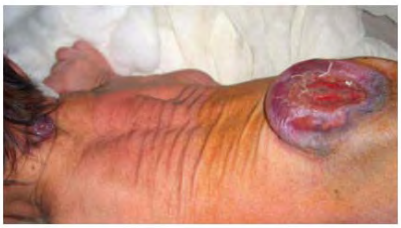


Figure 1. Lumbar myelomeningocele.

o Closed NTD

✓ Due to defect in secondary neurulation, and are confined to the spine.

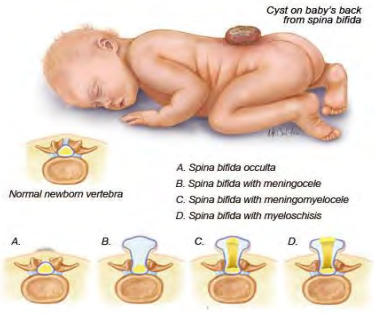
✓ Neural tissue is not exposed

✓ Defect is fully epithelialized (e.g. lipomyelomeningocele and tethered cord).

- Based on gross anatomic findings, which affecting
  - o Cranial structures, such as anencephaly and encephalocele,
  - o Spinal structures, such as spina bifida

Clinical presentation

- Cranial presentations :Anencephaly, encephalocele, and craniorachischisis totalis
- Spinal presentations: Spina bifida, myelomeningocele, congenital dermal sinus, lipomatous malformations, split-cord malformations, and caudal agenesis.
- Anencephaly: cerebrum, cerebellum, cranial vault are either reduced in size or absent.
  - o Meroacrania: if does not involve foramen magnum
  - o Holoacrania : if extends through foramen magnum
  - o Holoacrania with rachischisis: if anencephaly is accompanied by spina bifida.
- Spina bifida is a birth defect affecting the spinal column.
  - o 3 types: Spina bifida occulta, meningocele, spina bifida cystica (myelomeningocele)
  - o Disabling condition: Cognitive deficit, pulmonary function abnormalities; scoliosis; hip, foot, and leg deformities; bladder dysfunction; and short stature



- Myelomeningocele : 90% chance of having hydrocephalus, which causes cognitive deficits
- Cephalocele: herniation of the brain or meninges through a defect in the skull, associated with hydrocephalus, spastic quadriplegia, microcephaly, vision problems, mental and growth retardation, and seizures.

Epidemiology

- Balrampur district of Uttar Pradesh, India : 6.57~8.21 /1000 live births (highest worldwide)
- USA : 1.3/1000 (1970) → 0.6/1000 live births (1989)
- UK and Ireland : 4.5 /1000 births (1980) →1.0–1.5 /1000 births (1990s)
- Northern China : 79% reduction after addition of folic acid supplements to women's diets
- Australia → 2/ 1000 births (1990–1994) → 1.2 /1000 births (2009)
- *Anencephaly*
    - female-to-male ratio of 3:1, higher in older /very young mothers
    - After the first NTD-affected pregnancy, the risk of a subsequent NTD-affected pregnancy is almost tripled. However, 95% of the affected infants are born to parents with no family history of NTD.

Significance in clinical dentistry

Anencephaly

1. Craniofacial malformations :
   Hypoplastic or low-set ears or both; ocular proptosis; microphthalmia; subcutaneous nasal cleft; absent or incompletely-defined philtrum, cleft lip, cleft palate, bifid uvula, microstomia; and prominent maxillary alveolar ridges.
2. Thyroid gland: Normal, small, or larger in size
3. Cephalometrically,
    - Prognathic mandible
    - Hypothalamus is absent
    - Neurohypophysis is hypoplastic, which usually remains open
    - Cranial fossa: Anterior and middle are constricted laterally, and the posterior is increased in lateral extension, but constricted anteroposteriorly.
    - Sphenoid bone: The lesser wings are rudimentary and extend parallel to the midline
    - Frontal bone: The squamae are reduced in size and form most of the orbital roofs.
    - Vomer: The posterior height of the is increased, and the nasopharynx is enlarged.
    - Zygomatic bones: Rhomboid shaped in lateral view.
    - The cranial base angle is reduced, with a more vertically-oriented clivus.

Spina bifida

1. Hydrocephalus is a residual problem in patients with myelomeningocele and treated by shunt placement
2. Penicillin is commonly prescribed for shunt prophylaxis to prevent infective endocarditis in patients undergoing invasive dental procedures. Extractions and scaling/root planing are perceived to be high-risk procedures in patients with spina bifida.
3. The child is unable to open his mouth for a prolonged duration. Adaptive dental aids, such as a bite block, tongue retractor, and rubber dam, need to be used to control tongue movements and prevent swallowing of foreign materials.
4. The patient usually encounters difficulty sitting in the dental chair. Body position needs to be changed frequently to avoid pressure sores and uneasiness.

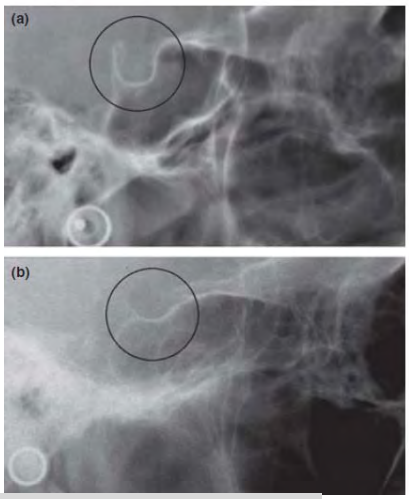
5. Most patients with spina bifida have lower limb deformities and might need to be treated in their wheelchair, or an assistant might be needed to help the child move to the dental chair.

Craniosynostosis in NTD

1. Facial bones are fused, resulting in a flat mid-face and protruding eyes. The patient exhibits a contracted upper jaw, resulting in a cross-bite and severely crowded teeth. Orthodontics and mid-face advancement might be done early in life or after growth completion, depending on the particular needs of the child

Sella turcica in myelomeningocele

1. The anterior wall of the sella is found to be obliquely oriented in an antero-posterior direction instead of following a normal cranio-caudal direction, giving an impression of a wide sella turcica with less depth than normal.



NTD and orofacial clefting

1. NTD occurs at a rate of 1:1000, and CLAP (cleft lip, alveolus, and palate) between 1:500 and 1:1500.
2. Both NTD and CLAP are known to be caused by a deficiency of folic acid and vitamin B6 during pregnancy, but do not occur in combination.
3. Both occur during the embryonal period, and are based on the closure failure of respective structures.
4. The combination of the two malformations is virtually never observed clinically, except in genetic syndromes, such as anophthalmia clefting NTD and Wildervanck syndrome.

NTD and Down syndrome

1. All or at least some cases of NTD and Down syndrome could have a common etiological pathway associated with impaired maternal folate metabolism.
2. Mothers of infants affected with NTD have an increased frequency of mutations in the genes encoding MTHFR, although not necessarily for Down syndrome.
3. The two have common epidemiological features, such as a large maternal contribution to both risk of occurrence and recurrence, increased number of miscarriages, ethnic differences, and maternal age.
4. Although the underlying mechanism for the connection between the disorders needs to be established, direct evidence of the link between the two implies that folate supplementation before conception can reduce the frequency of Down syndrome.

Diagnosis

- Obtaining the patient's history and conducting a physical examination and screening are essential.

- Differential diagnosis includes neonatal meningitis; spinal cord hemorrhage and infarction; spinal epidural abscess; staphylococcal, tuberculous, and viral meningitis; and cervical and lumbosacral disk syndromes.

Prevention and treatment

- Primary prevention:
  - In high-risk women, folic acid supplementation of 4 mg/day 3months before conception and during the first trimester is recommended
- Secondary prevention: screening
  - Maternal serum a-fetoprotein (MSAFP) test , high-resolution ultrasound , Amniocentesis
- Treatment:
  - Medical and surgical care by neonatologist, neurosurgeon, orthopedician, urologist.
  - Newborns with an open NTD should be kept warm, and the defect covered with a sterile saline dressing. Prompt closure of the defect should be done in a prone.

Conclusion

- NTD are of immense importance to the dental profession.
- The chances of increased caries, plaque, latex allergy, physical impairment, and anesthesia problems in spina bifida patients need to be considered.
- Alteration of the cranial base angle and prognathic mandible and sella turcica morphology can be predicted from cephalograms. Oral and maxillofacial surgeons and orthodontists have an important role in assessing craniofacial malformations and facial skeleton morphology, and treating craniosynostosis cases with appropriate surgeries.
- The association between NTD and conditions, such as cleft and Down syndrome, in some studies cannot be ignored.
- Therefore, dentists need to be well educated about these malformations, their etiology, screening, preventive measures, and relevance to the profession.

題號	題目
1	**What is the prevalence of orofacial clefting in Asian populations?** **(A) 1/5~1/10** **(B) 1/50~1/100** **(C) 1/500~1/1000** **(D) 1/5000~1/10000**
答 案 (C)	**出處：Oral and Maxillofacial Pathology, 3rd edition, P.3, by Neville/Damm/Allen/Bouquot**
題號	題目
2	**Which vitamin plays a role in neuronal function?** **(A) B** **(B) C** **(C) D** **(D) E**
答 案 (A)	**出處：Oral and Maxillofacial Pathology, 3rd edition, P.826, by Neville/Damm/Allen/Bouquot**