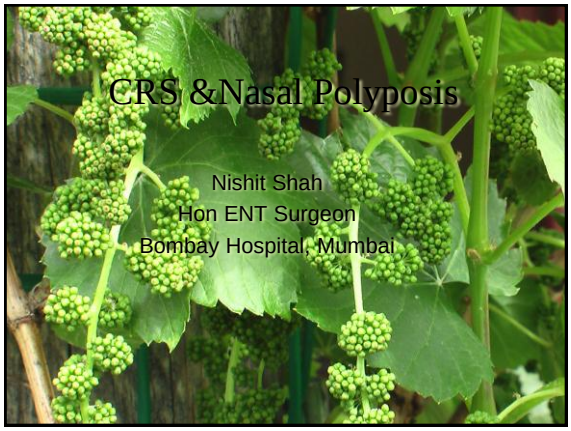

Nasal Polyps

- 2% of the population
- They are fluid filled sacs composed of an edematous tissue with infiltrating cells, including mast cells, eosinophils, lymphocytes and plasma cells surrounded by a ciliated airway epithelium- no true evidence of seromucinous glands
- An enigma !!!

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Aetiology

- Inflammatory
- Infection – bacterial, fungal, viral
- Allergic, Histamine
- Drug sensitivity
- Mechanical obstruction
- Mucopolysaccharide abnormality
- Autonomic imbalance, Enzyme abnormality
- Proto-oncogene, Laryngopharyngeal reflux

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Allergy

- Eosinophils are raised
- Presence of IgE & increased histamine levels
- 66% show no evidence of allergic disease
- Allergic rhinitis = children and young people
- Nasal polyposis = middle aged people
- Nasal polyps in allergic patients is usually under 5%, which is similar to that of the general population
- No evidence that H1 antihistamines are effective in nasal polyposis

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Inflammation

- Polyps originate from the nasal mucosa and were consistently related to sinus ostia
- Inflammation mediators consistently elevated
- Most theories & studies in support
- Opacification of the paranasal sinuses can be seen in the absence of polyps
- Most pts with rhinosinusitis do not have polyps

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Chronic Rhinosinusitis

With Nasal polyps	Without Nasal polyps
Activation of T2 helper cells	Activation of T1 helper cells
↓	↓
Release of cytokines IL 4, IL 5	Release of cytokine IL 8, INF
↓	↓
Eosinophil migration & activation	Neutrophil migration

OCNA 44 (2011) 685–695

Aetiology – Hypoxia & Exotoxins

- Hypothesized that hypoxia induces production of mediators that recruit cells into the sinus tissue and are involved in remodeling of the nasal mucosa.
- Evidence of exposure to staphylococcal exotoxins in the blood and polyp tissue of patients with CRSwNP. These exotoxins have the capacity to act as superantigens, bypassing normal antigen processing and directly stimulating a massive inflammatory response

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Fungus eosinophils

- Eosinophils leave the nasal tissue and migrate into the nasal mucus, degranulate and unload their toxic proteins, especially major basic protein onto fungal elements
- Histological examination – eosinophilic clusters as well presence of fungal elements within these clusters
- This eosinophilic cytotoxic mucin would lead to secondary epithelial damage in the mucosa lining

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Aetiology- Fungus or Mucin

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Associated Conditions

- 33% of patients with aspirin intolerance - Samter's syndrome or the aspirin triad-1968 (50% - alcohol)
- 7-17% of patients with asthma
- 2% of patients with chronic rhinosinusitis
- 50% of the eosinophilic vasculitis of Churg Strauss Syndrome
- 85% of patients with AFS
- 20% of patients with NARES
- 20% of patients with cystic fibrosis
- Young's syndrome, Kartagener's syndrome (tissue lymphocytes)

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Pathogenesis

- Contact areas & narrow clefts that create turbulent flow of air in the lateral wall of the nose, particularly when narrowed by mucosal inflammation
- Viral-bacterial-fungal-host interactions- inflammation
- Ulceration and prolapse of the submucosa with reepithelialization and new gland formation
- A polyp forms as inflammatory process from epithelial cells, vascular endothelial cells, and fibroblasts affects the bioelectric integrity of Na+ and Cl- channels

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Pathogenesis

- Results in an increased movement of water into the cell and into the interstitial fluid
- Leads to growth and enlargement of the nasal polyp which is self perpetuating
- Rapid recurrence - some intrinsic phenotypic characteristic of nasal epithelial cells in the lateral wall of the nose, which is likely to be under genetic control

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Pathogenesis

- Several haemopoietic and pro-inflammatory cytokines (GM-CSF, IL-5, IL-6, IL-8, SCF) are upregulated in various tissue compartments (epithelium, stroma) of nasal polyps
- Thus, nasal polyps can be looked upon as a type of self-perpetuating inflammatory process
- IL-4 induces fibroblast proliferation and formation of abundant stroma

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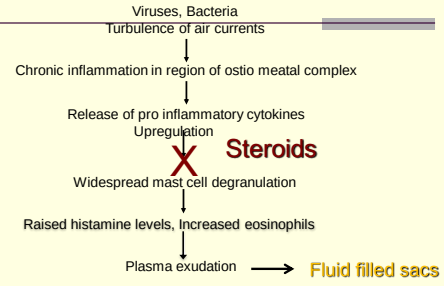
Aetiology: self perpetuating inflammatory process



Symptoms

- Nasal obstruction
- Recurrent sinusitis
- Hyposmia
- Headache
- Rhinorrhœa, Postnasal drip
- Sneezing
- Snoring

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Examination

- Polyp – polyps – misc
- Palpation
- Site
- Size
- Extent
- Associated conditions
- DNE
- Respiratory System

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Examination

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Differential Diagnosis

- Ethmoidal polyps, A-C polyp
- Encephaloceles, Gliomas, Meningiomas
- Dermoid tumors, Hemangiomas
- Papillomas, Inverting papillomas
- Juvenile nasopharyngeal angiofibroma
- Lymphomas
- Rhabdomyosarcoma, Nasopharyngeal carcinoma
- Neuroblastomas, Sarcomas, Chordomas

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Investigations

- DNE
- CTScan, MRI, Cisternography
- Allergy tests
- Sweat chloride test or genetic testing for CF in any child with polyps
- Nasal smear for eosinophils & neutrophils may differentiate allergic from nonallergic
- Routine

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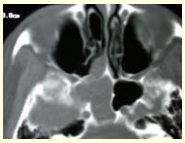
Radiology



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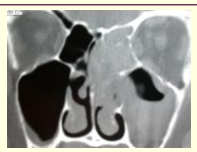
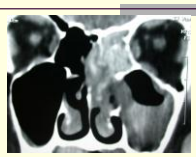
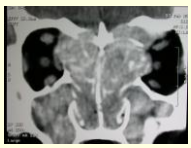
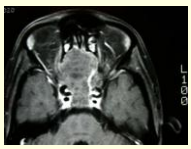
Radiology

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Medical Rx

- Steroids
  - Oral – Topical
- Antibiotics
- Anti-fungals
  - Oral – Topical
- Anti-histamines
- Decongestants
  - Oral – Topical
- Anti-inflammatory

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Corticosteroids

- Corticosteroids are the only drugs with a proven effect – medical polypectomy
- Relieve symptoms by downregulating the expression and production of cytokines such as IL-5 which effectively reduces the number of eosinophils
- At five months, the majority of them relapsed
- Neutrophil polyps do not respond well (CF, primary ciliary dyskinesia)

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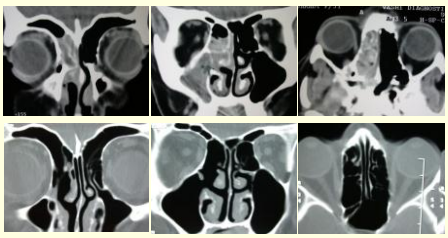
Medical Polypectomy



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Topical Steroids

- Steroids bind to cytoplasmic glucocorticoid receptors, modify gene transcription inducing a change in cellular protein synthesis
- Inflammatory reaction in nasal polyposis is in part driven by T lymphocytes and the cytokines products they produce
- Topical steroids reduce the total number of T lymphocytes in nasal polyp tissue
- Reduce the number of activated eosinophils, but not mucin expression in polyps

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Nasal steroid sprays

- Fluticasone proprionate / furoate
- Mometasone, Ciclosanide
- Safe to use for years
- May take 6 weks for max benefit
- Good for control & post-op
- Not great in reducing polyp bulk
- Useful for olfactory recess polyps

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Leukotrine Inhibitors

- Inflammatory molecules from arachidonic acid, the precursor of prostaglandins
- 2 groups – neutrophil & eosinophil dependent
- Zileuton – leukotriene inhibitor
  - dosed four times a day at 600 mg
- Montelukast & zafirulast – leukotriene receptor antagonists
  - Montelukast – once a day at 10 mg (5 mg between the ages of 6 and 14
  - Zafirulast is given twice a day at 20 mg without food

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Anti-fungal Rx

- Amphotericin B: 1% suspension;
- Antifungal nasal lavages – 20 ml/each/bd
- Fungicide nasal spray - 400 µl/ bd
- 39 – 43% Total Disappearance
- 48 – 64% post-op pts
- Hyper-reactivity to fungus
- Direct effect on the integrity of the cell membranes of the polyp epithelium
- Oral – Itraconazole – Voriconazole, Fluconazole

Alma Ricchetti et al, Geneva

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Macrolide Treatment

- Long-term macrolide treatment
- 150 mg/day for 2-3 months
- Polyp patients with chronic rhinosinusitis
- Decreased the amount of IL-8 production in nasal polyps as well as decreased the size of the polyps
- IL-8 is particularly common in the neutrophilic type of polyps as in cystic fibrosis

Ichimura - Yamada – Japan

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Surgery with a Debrider

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Antral polyp

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Recurrence

- The degree of tissue eosinophilia appears to be an important denominator of the recurrence rate of nasal polyps.
- In non-eosinophil dominated inflammation (cystic fibrosis, primary ciliary dyskinesia) other pathophysiological mechanisms may be of importance
- Complete surgical clearance
- Associated medical Rx

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Recurrence

- mRNA of IL-1ß,IL-6, IL-8, MCP-1 and TNF-· as well as pLT and PGE2 levels are detectable and appear to play a role in the persistence of inflammation in CRS.
- Their level decreases only insignificantly over time, even in the absence of acute exacerbation of disease
- Thus rendering the mucosa possibly more prone for recurrent acute episodes

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Recurrence

- 75% at 6 years PO (Jones) 35% (Shah)
- Incomplete Surgery
- Stenosis of Ostia
- Retained mucus
- Poor follow-up
- Lack of adjuvant medical treatment
- Failure to recognize aetiology

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Summary

- Aetiology
- Pathogenesis
- Mediators
- Investigation
- Medical treatment
- Pre-op prepartaion
- Surgery
- Post-op follow up

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Future

- Steroid nasal spray that is specific to raising levels of CC10 gene
- Local anti-fungal sprays
- Anti – leukotrines – mediaters
- Genetic
- Surgery ?????

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Thank You
Dr Nishit Shah