

Autoimmune Inner Ear Diseases



Abdul-Rahman Hagr
MBBS FRCS_c

Objectives

- ◆ Cases
- ◆ Physiology of inner ear immune function
- ◆ Autoimmune inner ear disorders
- ◆ Diagnosis
- ◆ Treatment

Objectives

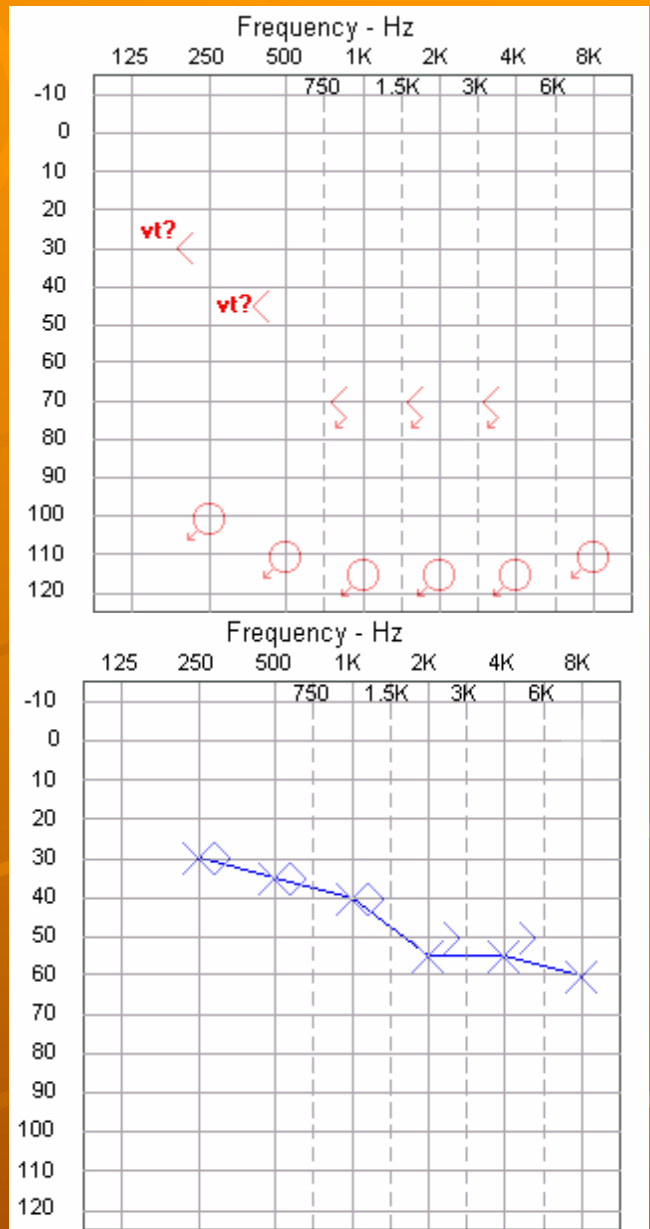
◆ Cases

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- ◆ Treatment

Contralateral Delayed Endo-Lymphatic Hydrop CDEH

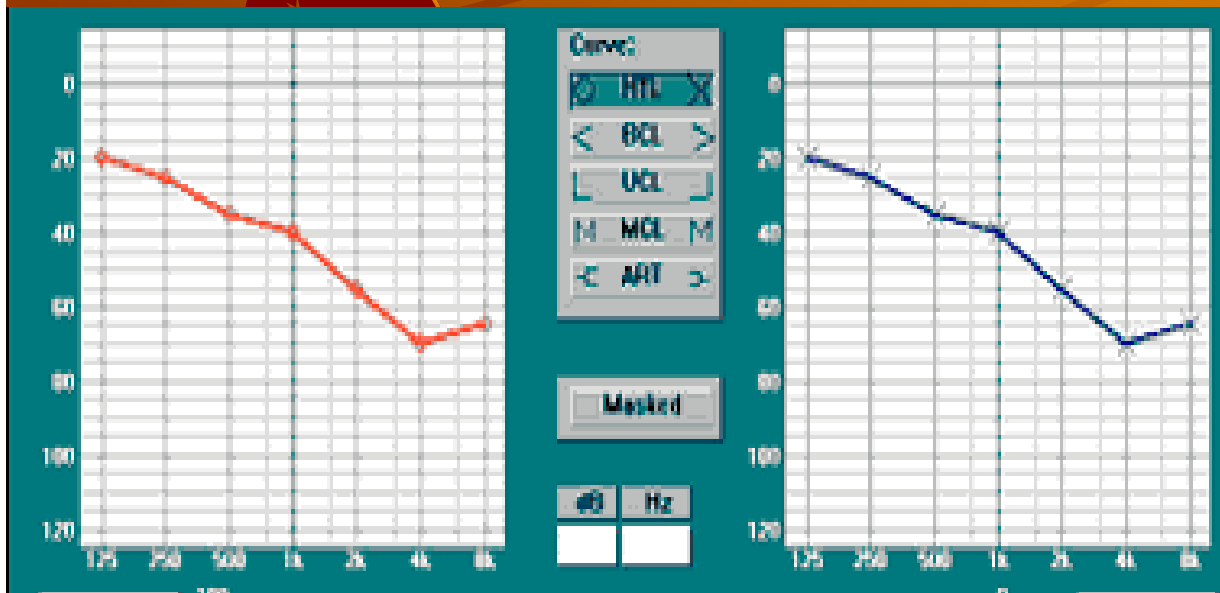
- ◆ 50 Y Female
- ◆ Rt ear Trauma 10 Y
- ◆ Lt ear
 - Fluctuating HL
 - Tinnitus
 - Vertigo

Sympathetic Labrynthitis



Polyarteritis Nodosa

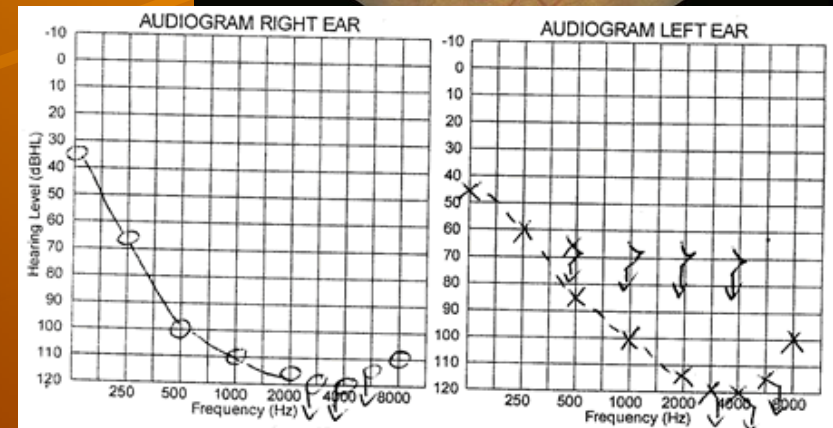
- ◆ 50 y
- ◆ Arthritis
- ◆ Skin nodules
- ◆ Bil SNHL



Vogt-Koyanagi-Harada (VKH) Syndrome

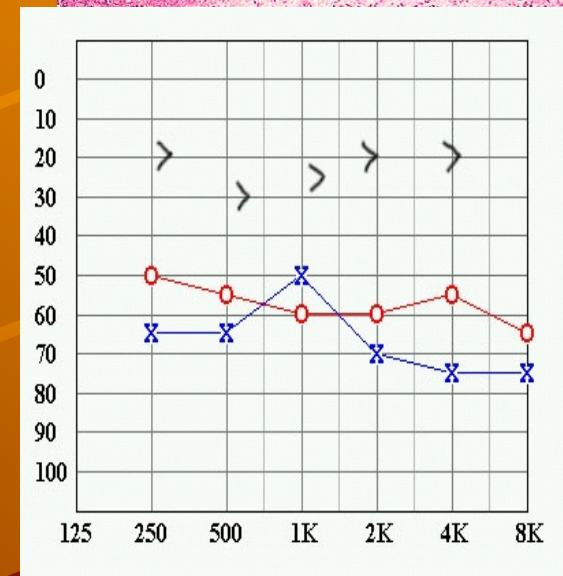
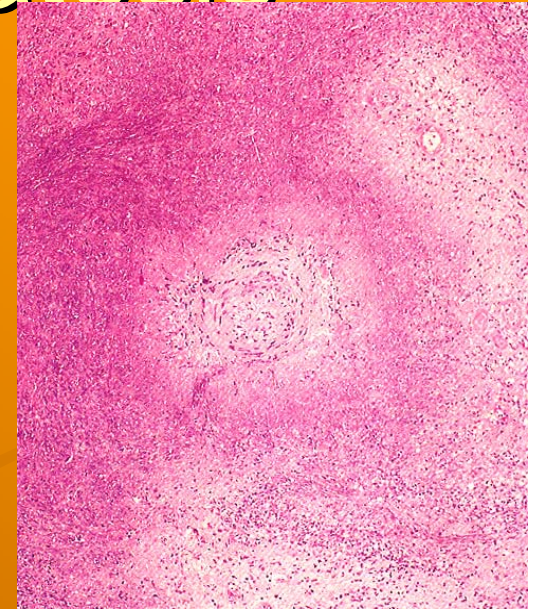
- ✦ 30 y female
- ✦ SNHL for CI assessment*
- ✦ Vertigo
- ✦ Visual loss
- ✦ Morning headache
- ✦ Projectile vomiting
- ✦ CSF: High WBS
-ve culture

*D/Dx



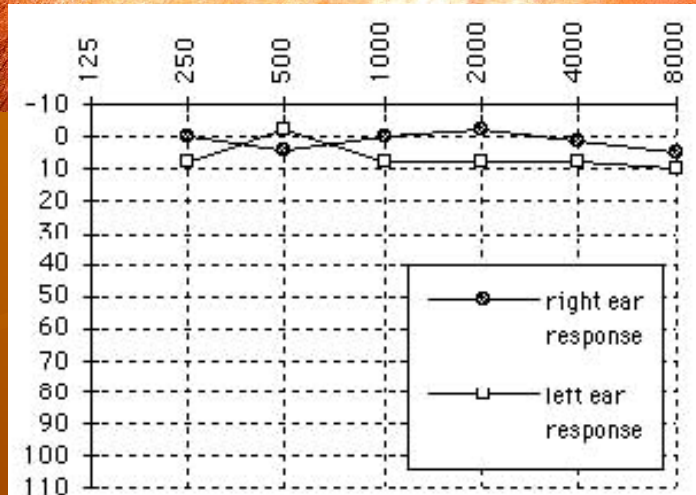
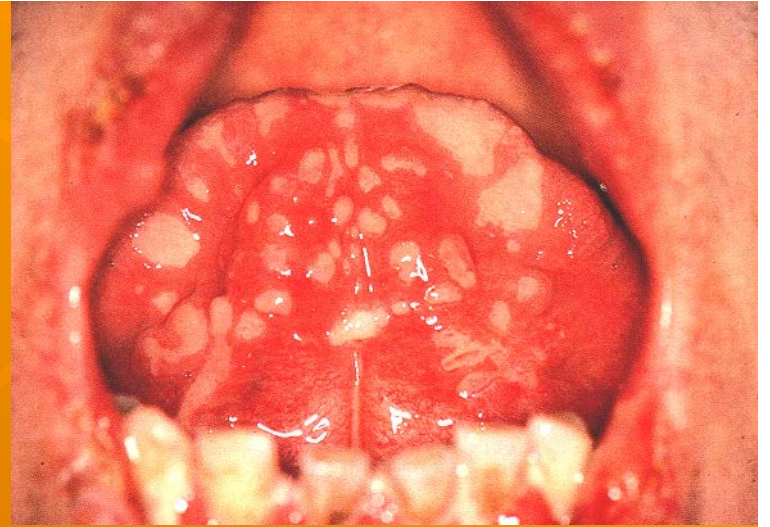
Wegener's Granulomatosis

- ✦ 50 y female
- ✦ serous OM
- ✦ Nasopharyngeal mass →
- ✦ Histopathology
 - Necrosis*
 - Granulomata
 - vasculitis



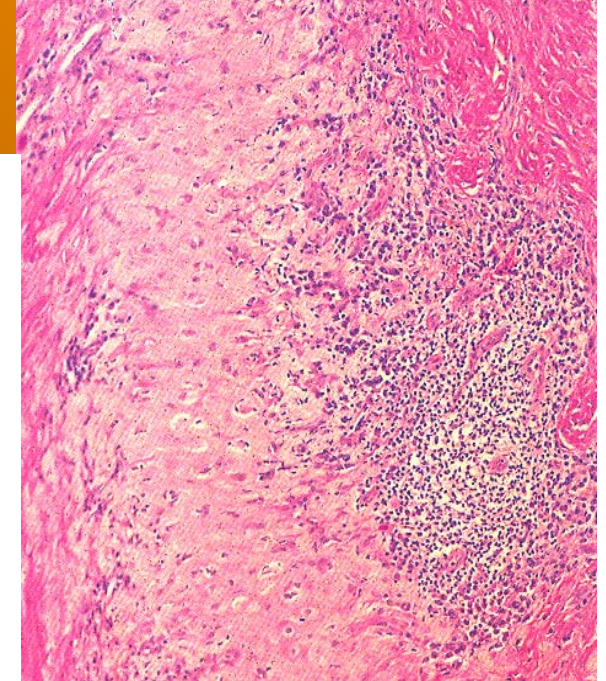
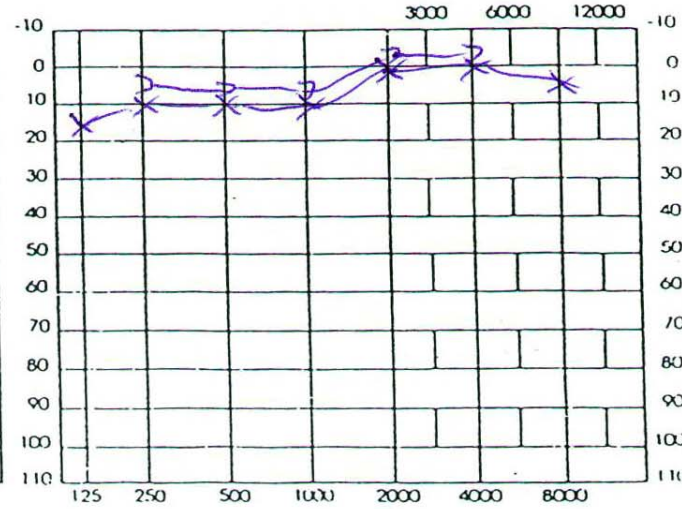
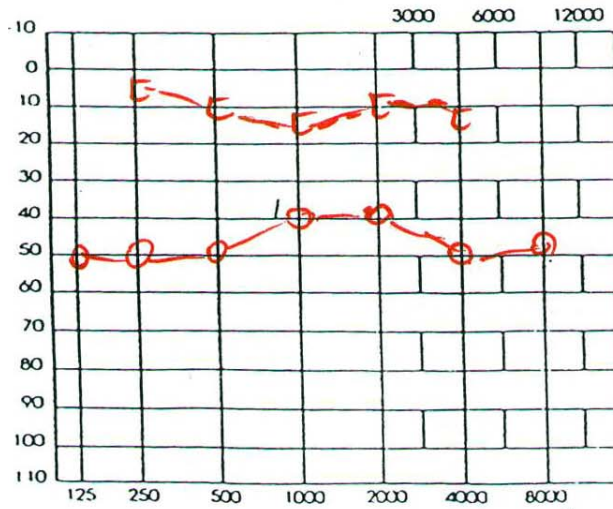
Behçet's Disease

- 50 y male
- Bil HL get better with steroid
- Arthritis
- Genital and oral ulcer



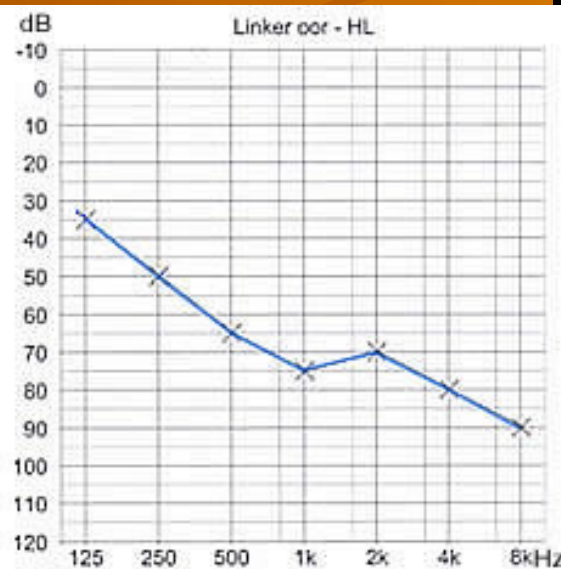
Relapsing Polychondritis

- ✦ 30 y male
- ✦ Nose deformity
- ✦ Bi-phasic Stridor
- ✦ Bil fluct- SNHL
- ✦ Rec ear swelling
- ✦ Persistent Rt HL
- ✦ +ve VDRL -ve FT-ABS



Systemic Lupus Erythematosus

- 30 y female
- Mouth ulcers
- Skin rash
- Arthritis
- Rt SSNHL
- Lt long Hx SNHL



Rheumatoid Arthritis

- ◆ 50 Y Female
- ◆ Morning stiffness
- ◆ SNHL
- ◆ Arthritis
- ◆ -ve RF



Churg-Strauss Syndrome

- ◆ 52 y male
- ◆ AR & BA
- ◆ HL
- ◆ Skin rash
- ◆ CBC High eosinophil



Kawasaki Disease

- ◆ 4 y boy
- ◆ HL
- ◆ Fever
- ◆ Rash
- ◆ Cervical lymphadenopathy
- ◆ Chest pain
- ◆ Died in ICU



Objectives

- ◆ Cases
- ◆ Physiology of inner ear immune function
 - Hyper-sensitivity
 - Inner Ear Immunology
- ◆ Autoimmune inner ear disorders
- ◆ Diagnosis
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Types of Hypersensitivity

(ACID-R)

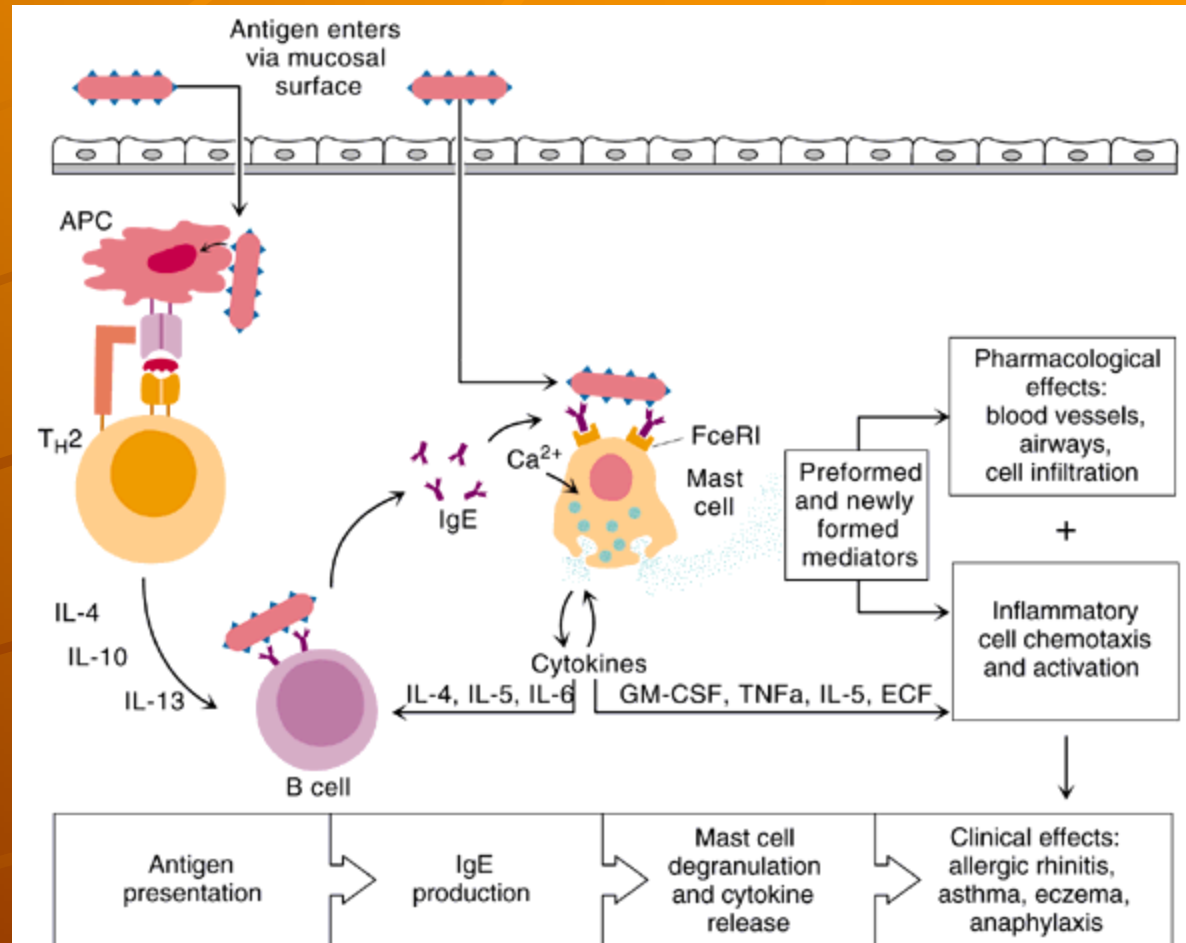
- ◆ Type I Anaphylaxis
- ◆ Type II Cyto-Toxic
- ◆ Type III Immune-Complex
- ◆ Type IV Delayed cell mediated
- ◆ Type V Receptor



Hypersensitivity Reaction	Type I	Type II	Type III	Type IV
Synonym	Anaphylaxis (immediate type)	Cytotoxic (Antibody-dependent)	Immune-complex initiated	Cell-mediated (delayed)
Time elapsed	~Seconds to minutes	~Hours to a day	~Hours to days	~2-3 days
Specific immune	IgE	IgG, IgM	IgG, IgM	T cells reactant
Chemical mediators of tissue injury& inflammation	Vasoactive products of mast cells/ basophils (histamine, arachidonate derivatives)	Complement (C')	C' (cytolytic, chemotactic, vasoactive components)	Lymphokines/ monokines
Cell pathology/ pathophysiology	Accumulation of neutrophils, eosinophils. Smooth muscle contraction.	Phagocytosis, lysis of target (Rbcs, platelets, Wbcs, GBM). Receptor dysfunction*	Accumulation of neutrophils, macrophages. Release of lytic lysosomal enzymes	Lymphocytes & macrophages; granulomas
Clinical examples	Anaphylaxis Atopic disorder (Allergic rhinitis, Hay fever, Bronchial asthma, Atopic dermatitis) Urticaria. Angioedema	Autoimmune hemolytic anemia. Transfusion reaction. Hemolytic disease of new born. Immune thrombocytopenia. Goodpasture's syndrome. Myasthenia gravis.* Graves' disease*	SLE (nephritis, vasculitis). IC GN. SBE. Serum sickness.	Granulomatous disease (Tuberculosis, Leprosy, Sarcoidosis). Contact dermatitis (Poison ivy). Hashimoto's thyroiditis. IDDM. Organ allograft rejection.

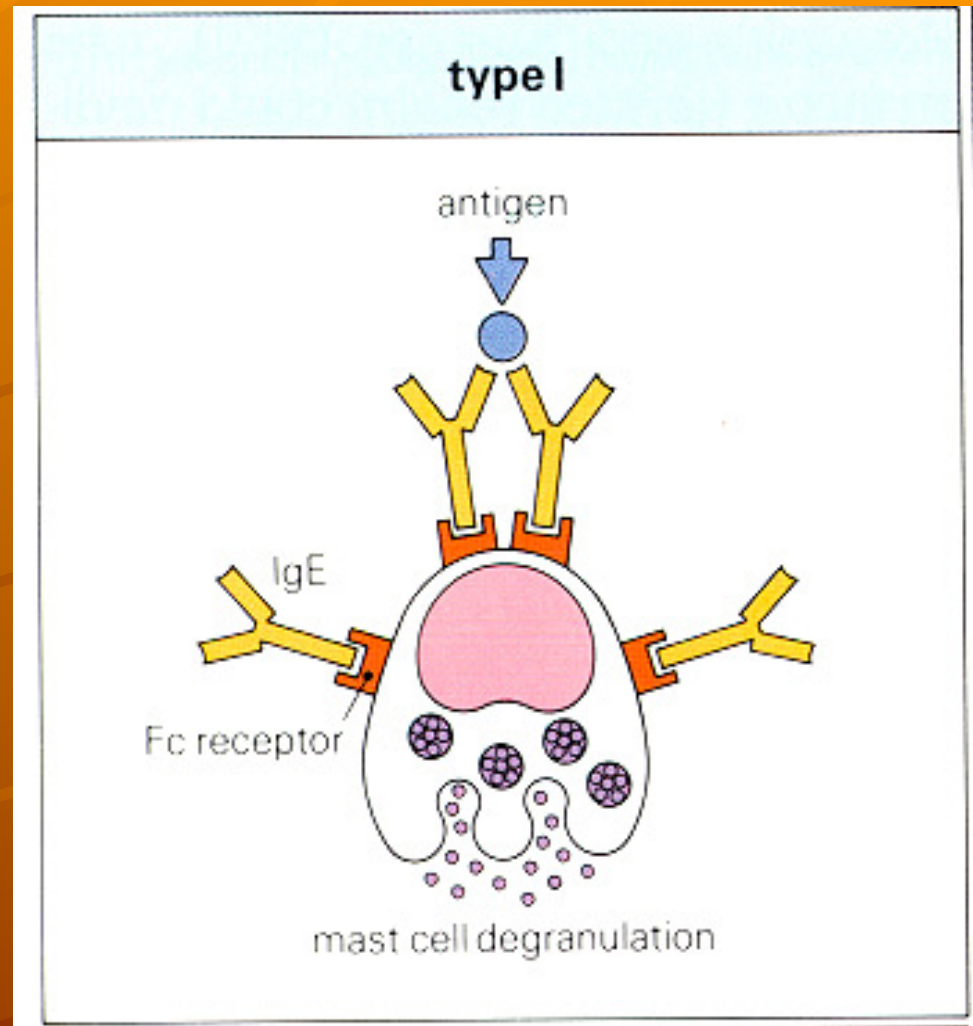
Type I Hypersensitivity

- ✦ IgE
- ✦ mast cells
- ✦ histamine
- ✦ vasodilation
- ✦ ? Hydrops
- ✦ Meniere's

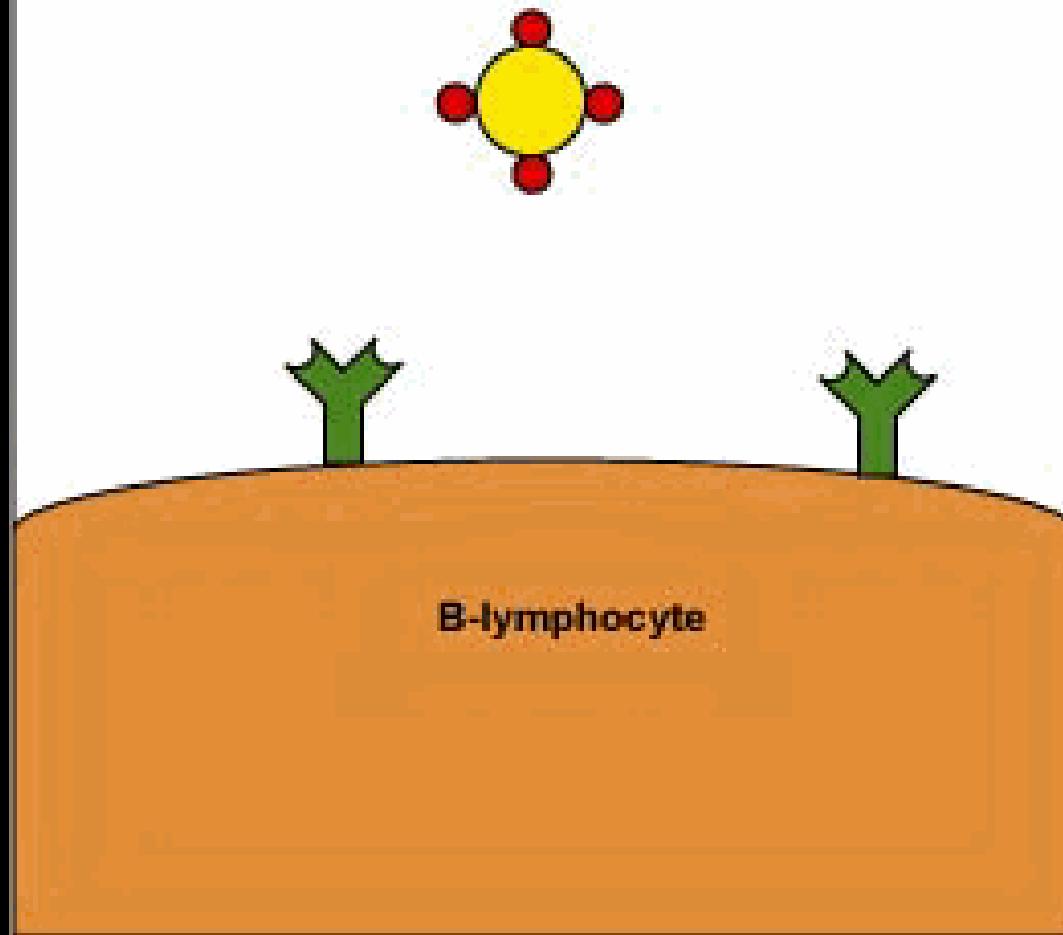


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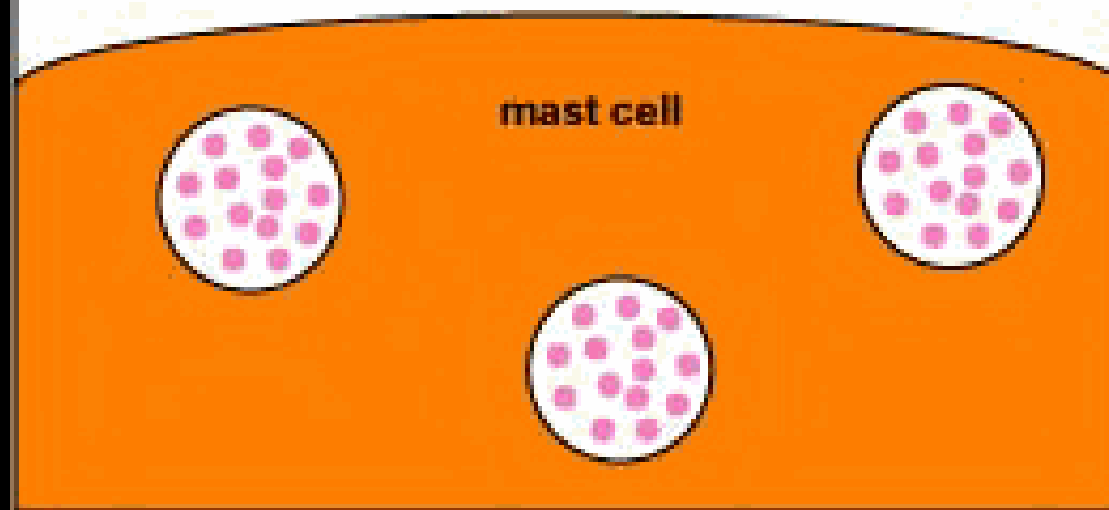
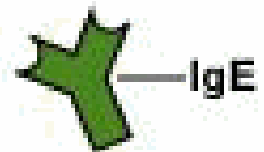


**Binding of Allergen to B-cell Receptor
on B-lymphocyte**



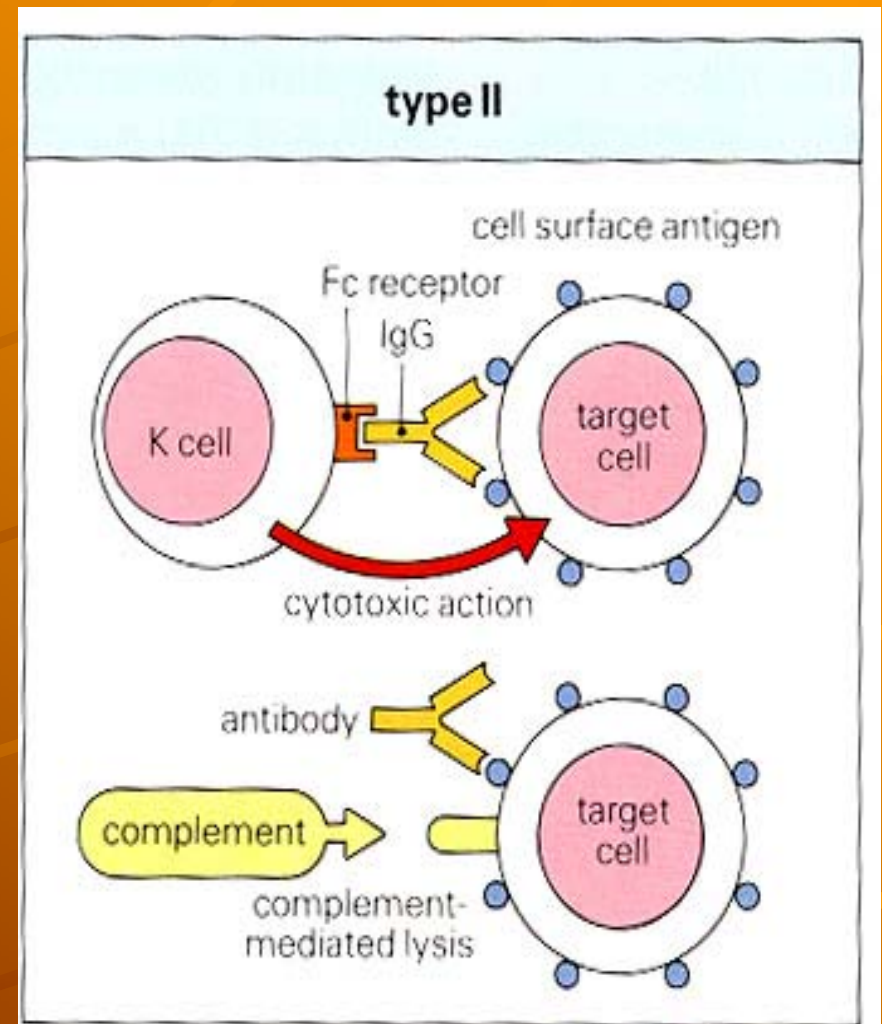
<http://www.cat.cc.md.us/courses/bio141/lecguide/unit1/bacpath/hypersen/hypersen.html#typeiii>

Binding of IgE to Receptors on Mast Cells

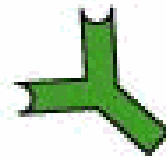


Type II Hypersensitivity

- ✦ Antibodies
- ✦ complement activation
- ✦ HSP-70
- ✦ SLE

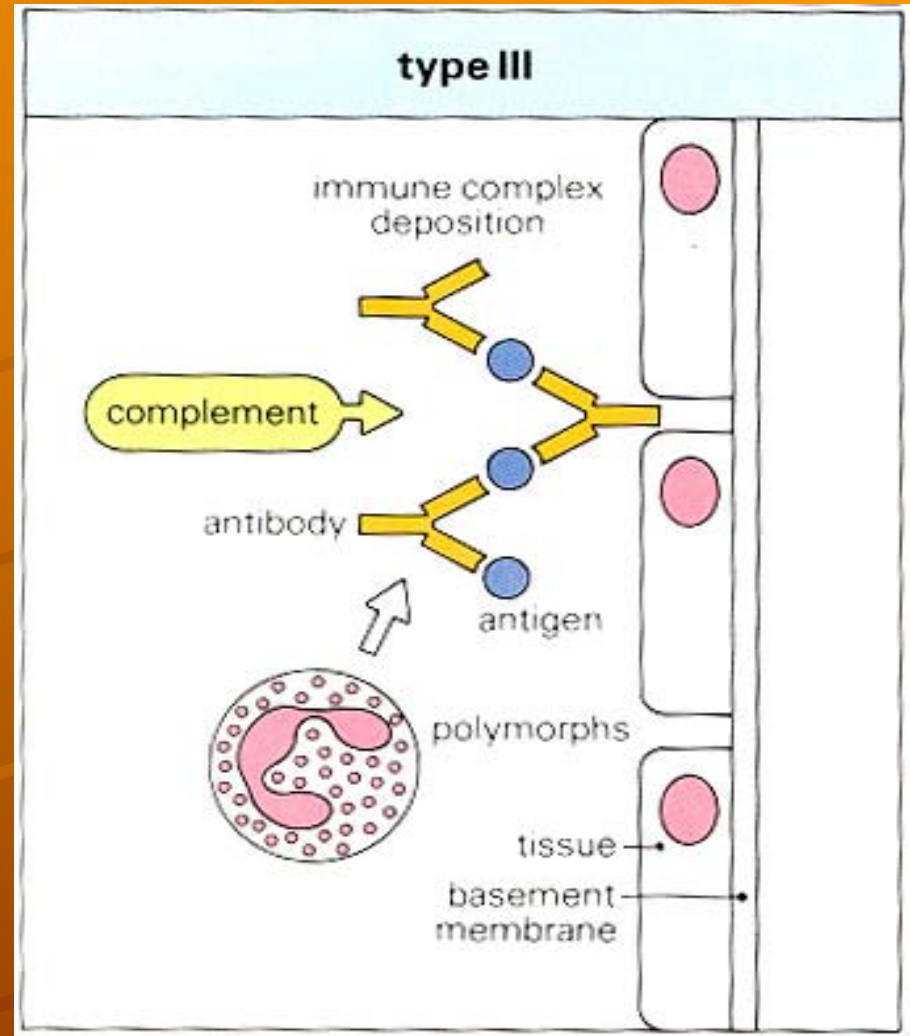


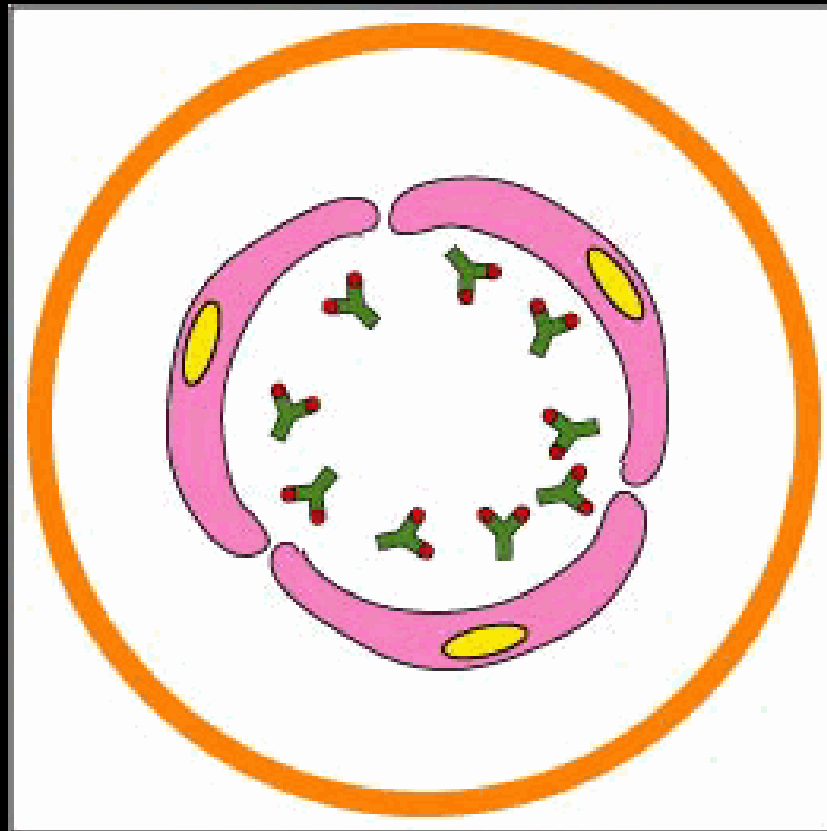
normal cell



Type III Hypersensitivity

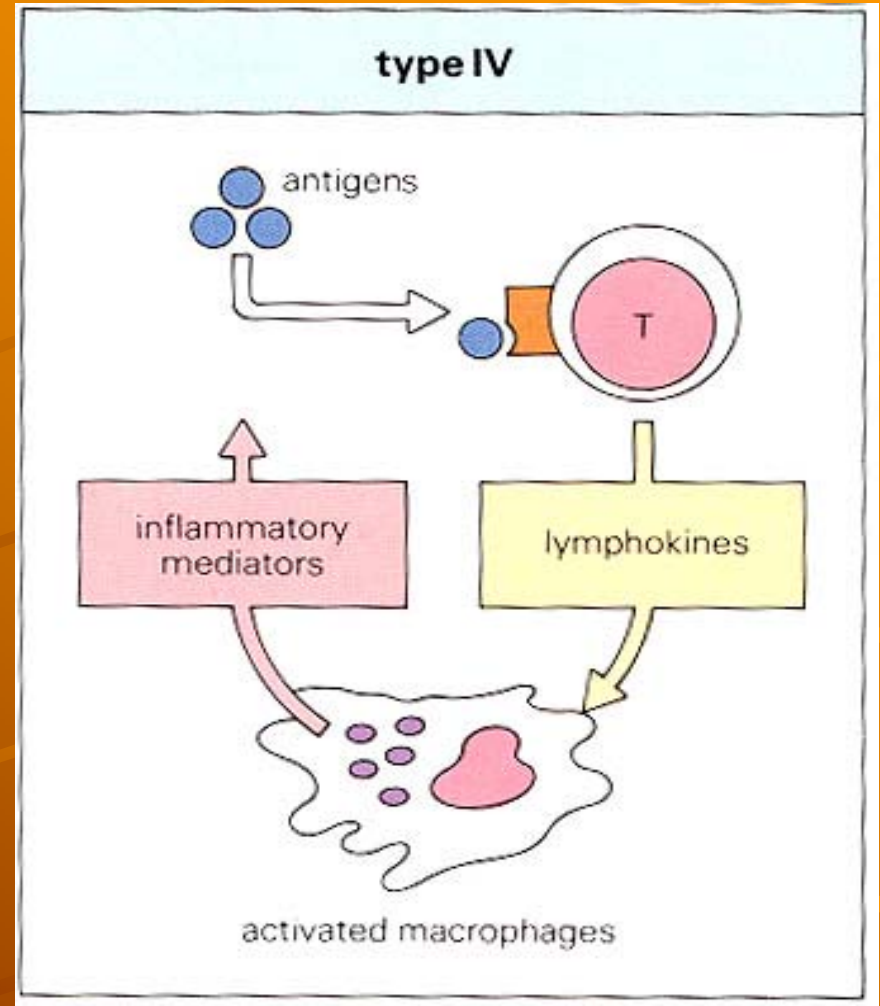
- ◆ Immune complex
- ◆ Ig deposition
- ◆ Vasculitis
- ◆ Tissue injury
- ◆ Wegener's,
?Meniere's





Type IV Hypersensitivity

- ✦ T-cell mediated
- ✦ direct lysis
- ✦ lymphokine production
- ✦ Cogan's syndrome



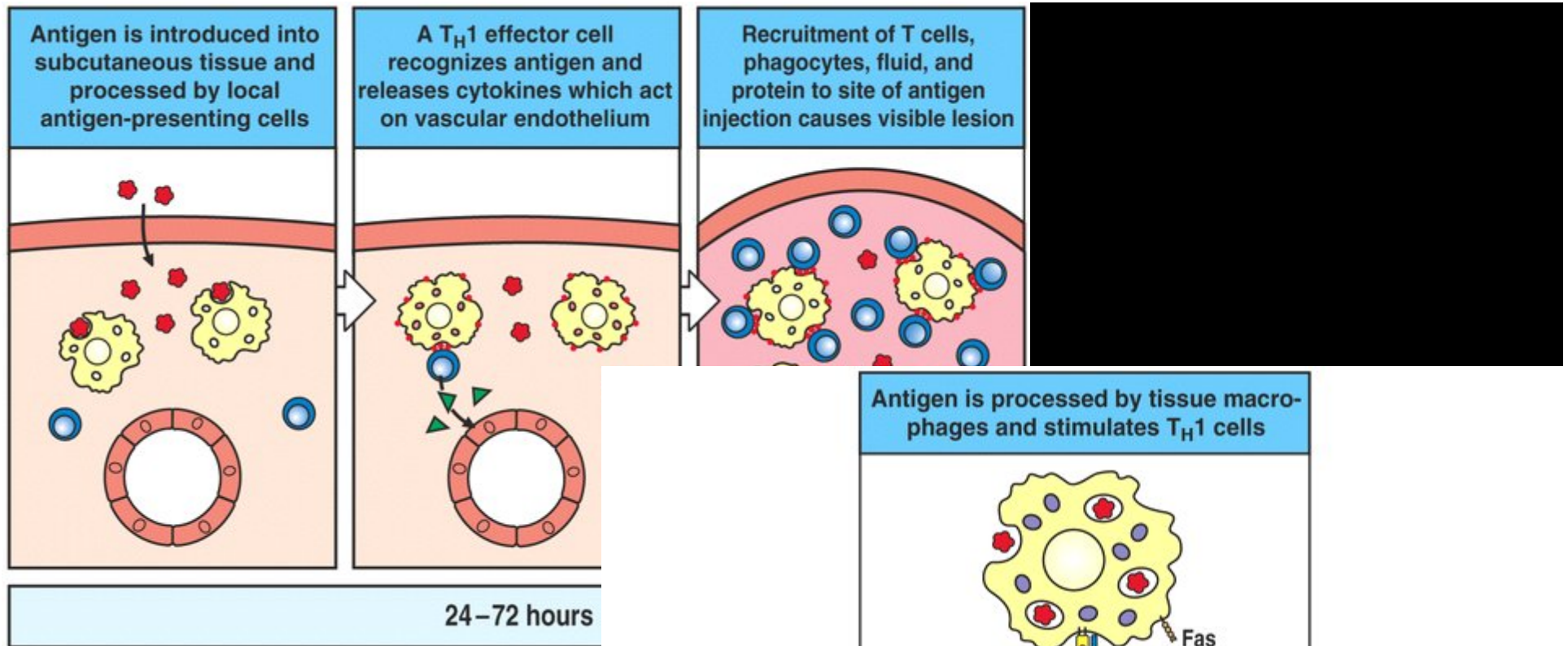


Figure 10-34 The Immune System, 2/e (© Garland Science 2005)

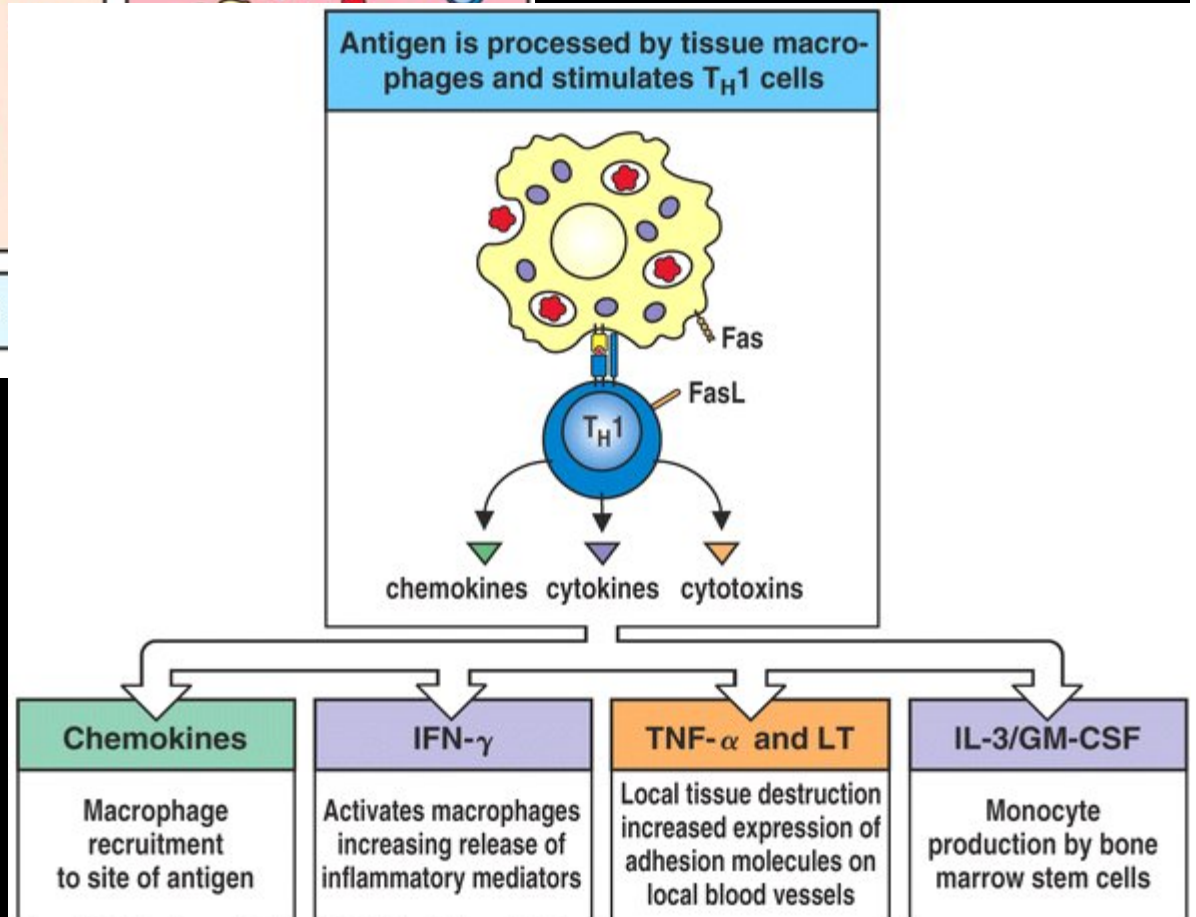
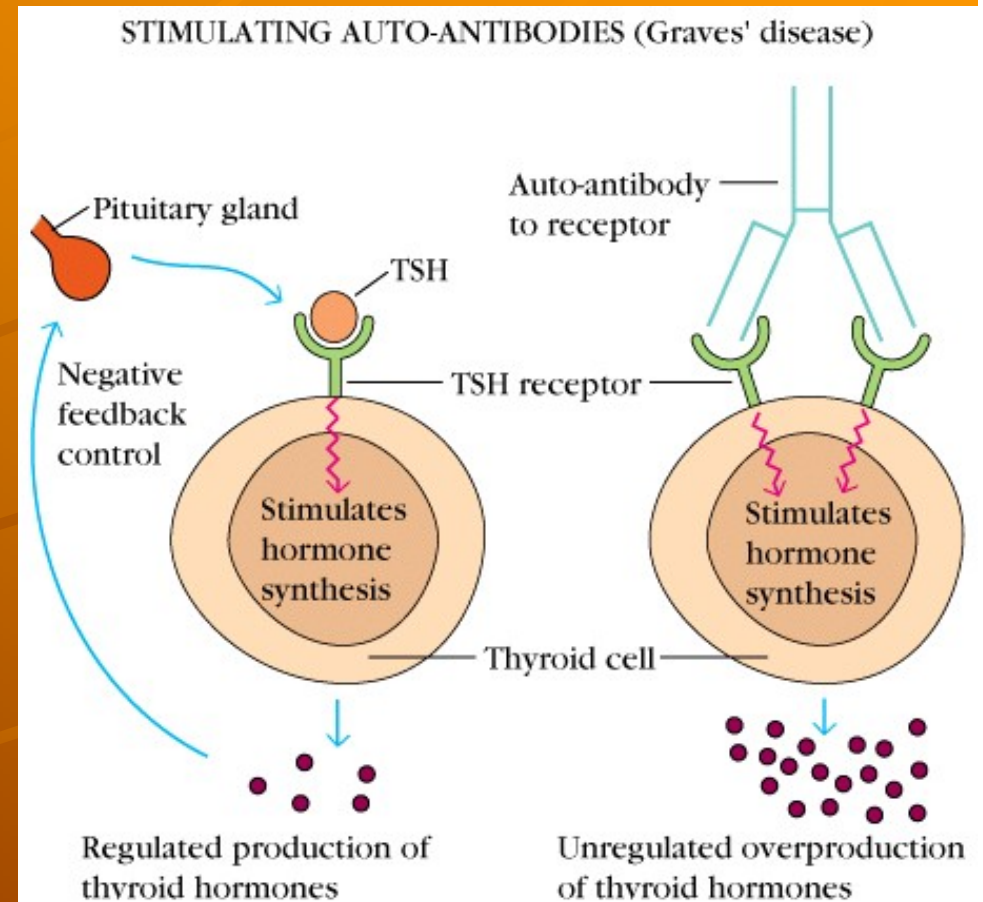


Figure 10-35 The Immune System, 2/e (© Garland Science 2005)

Type V Hypersensitivity

- ✦ Receptor
- ✦ Block or stimulate
- ✦ Ex:
 - Hashimoto's
 - Myasthenia G
 - Grave's



Examples of autoimmune disease

Graves' Disease (thyrotoxicosis)

Hashimoto's thyroiditis

pernicious anaemia

Addison's disease

insulin dependent diabetes mellitus

Goodpasture's syndrome

myasthenia gravis

multiple sclerosis(?)

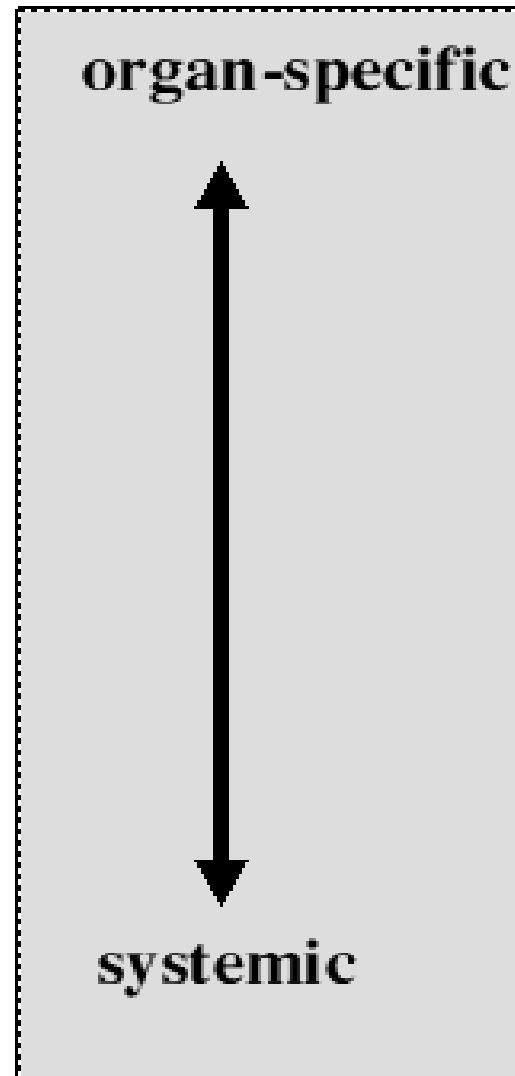
autoimmune haemolytic anaemia

idiopathic thrombocytopenic purpura

rheumatoid arthritis


scleroderma

systemic lupus erythematosus (SLE)

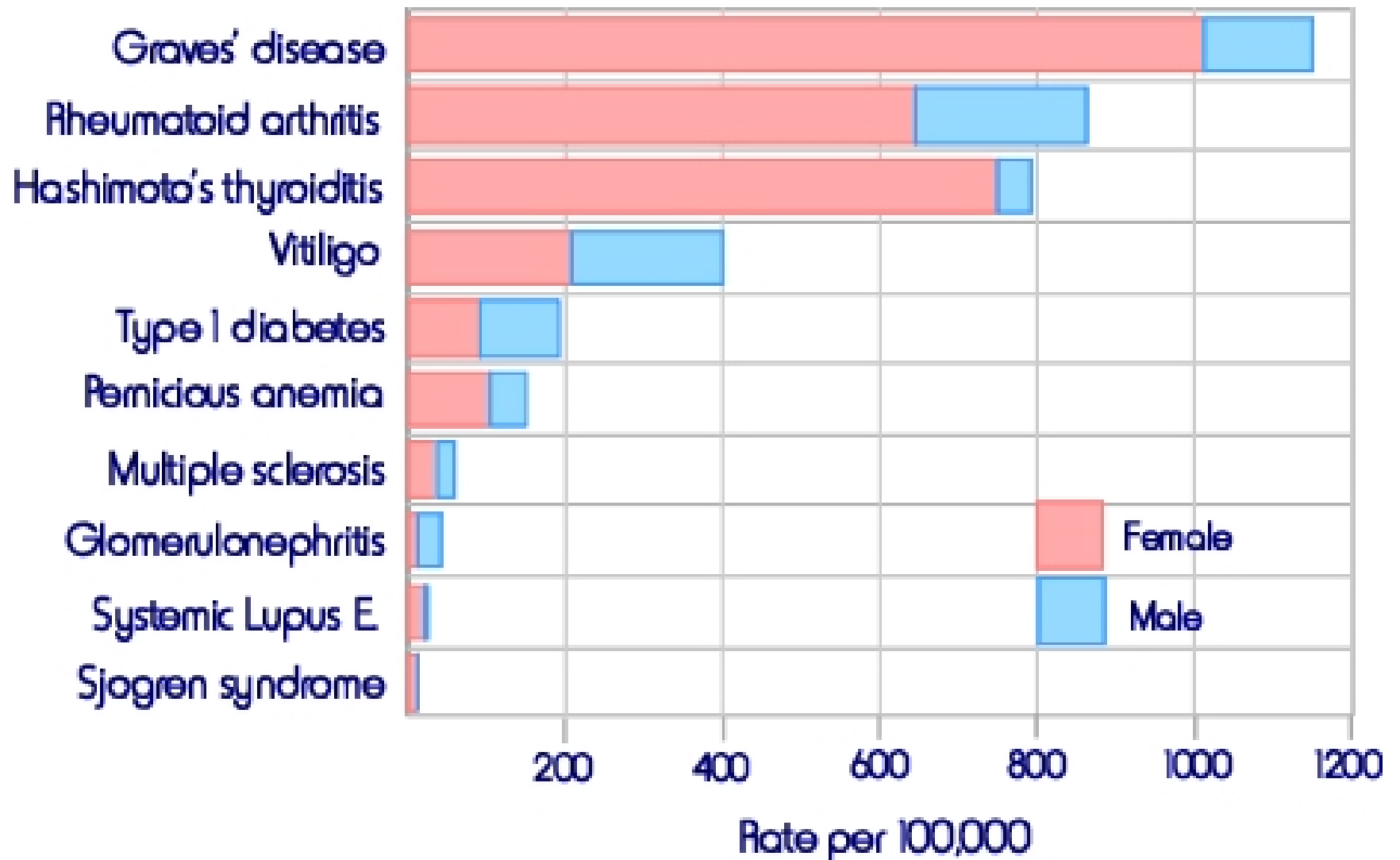


The spectrum of autoimmune disease

Organ Specific Autoimmune Diseases

- 
- Graves Disease (Thyroid: TSHR Abs, TPO Abs)
 - Hashimoto Thyreoiditis (Thyroid: TPO Abs, Tg Abs)
 - Diabetes Type I (Pankreas: GAD II Abs, IA2 Abs, ICA)
 - Goodpasture Syndrome (Kidney: GBM Abs)
 - Pernicious Anemia (Stomach: Parietal Cell Abs)
 - Primary Biliary Cirrhosis (Liver, Bile: AMAbs)
 - Myasthenia Gravis (Muscles: AChR Abs)
 - Dermato-/Polymyositis (Skin / Muscles: Jo 1 Abs)
 - Vasculitis (Vessels: ANCA)
 - Rheumatoid Arthritis (Joints: CRP, RF, RA33 Abs, Sa Abs)
 - MCTD (RNP Abs)
 - Scleroderma (Scl 70 Abs, CENP Abs, PM/Sci Abs)
 - SLE (ANA, Cardiolipin Abs, Beta 2 GP I Abs)

Multi-systemic Autoimmune Diseases



Objectives

- ◆ Cases
- ◆ Physiology of inner ear immune function
 - Hyper-sensitivity
 - *Inner Ear Immunology*
- ◆ Autoimmune inner ear disorders
- ◆ Diagnosis
- ◆ Treatment

Introduction - AIED

McCabe 1979

- ✦ first described AIED
- ✦ Series of 18 patients
- ✦ Bilateral, rapidly progressive SNHL
- ✦ 100% had a + Lymphocyte transformation test (LTT) compared to 0% in controls
- ✦ Hearing improved with steroids
- ✦ One temporal bone showed vasculitis

Bilateral, rapidly progressive SNHL improved with steroids

Antigens

- ◆ Harris 1990

- Used Western blot to discover anti 68kDa autoantibody in sera of patients with Idiopathic sudden or RPSNHL (HSP-70)

- ◆ Multiple other candidate antigens have been proposed

- Type II Collagen (Yoo et al., 1982)
- Beta tubulin (Connolly et al., 1997)
- 30 kDa protein
- c Raf

Inner Ear Immunology

- ✦ Blood-labyrinthine barrier
 - Little lymphatic drainage
 - Immunoglobulins 1/1000th of serum
 - Cochlea is devoid of immune cells
- ✦ Endolymphatic sac
 - contains immunocompetent cells
 - Site of Ag processing in the inner ear
 - Protects from immunologic damage

Immune Function of Inner Ear

✦ Sterile labyrinthitis studies

- I.E can generate a local immune response
- responses depend on the presence of E-Sac
- Cells that mediate the labyrinthitis enter the scala tympani via the spiral modiolar vein
- Labyrinthitis → loss of sensory cells → fibrosis and osteoneogenesis

Animal models

- ✦ Elevations in auditory thresholds
- ✦ Degeneration of the stria vascularis
- ✦ Antibody deposition within the strial capillaries
- ✦ Absence of inflammatory response.
- ✦ Corticosteroids improves hearing without impeding the development of the morphologic changes
- ✦ Improvements due to the mineralocorticoid effects on the cochlea, not due to immunosuppression

Lacking Evidence

- No Ag found as a single target of autoimmunity
 - Candidate antigens proposed
 - 68 kDa protein linked to hsp 70
 - Type II collagen
- Histopathology
 - Unable to exam T-bone during disease activity
 - fibrosis and osteoneogenesis



Lacking Evidence

- ✦ Response to immunosuppression
 - Animals pretreated with cyclophosphamide prior to viral insult have reduced hearing loss (Darmstadt et al.)
- ✦ No study has yielded an animal model that is definitively analogous the human condition.



Objectives

- ◆ Cases
- ◆ Physiology of inner ear immune function
- ◆ **Autoimmune IE disorders**
- ◆ Diagnosis
- ◆ Treatment

Autoimmune SNHL

◆ Non-Organ specific

- Polyarteritis nodosa
- Vogt-Koyanagi-Harada
- Cogan's syndrome
- Wegener's granulomatosis
- Relapsing Polychondritis
- Systemic Lupus Erythomatosus
- Rheumatoid Arthritis
- Churg-Strauss Syndrome
- Kawasaki Disease

◆ Organ specific

- Meniere's Disease
- Contralateral Delayed Endo-Lymphatic Hydrop

Polyarteritis Nodosa

- ◆ Vasculitis of small and medium-sized arteries renal and visceral
- ◆ Ischemia
- ◆ Osteoneogenesis
- ◆ fibrosis
- ◆ hearing loss rare (1%)



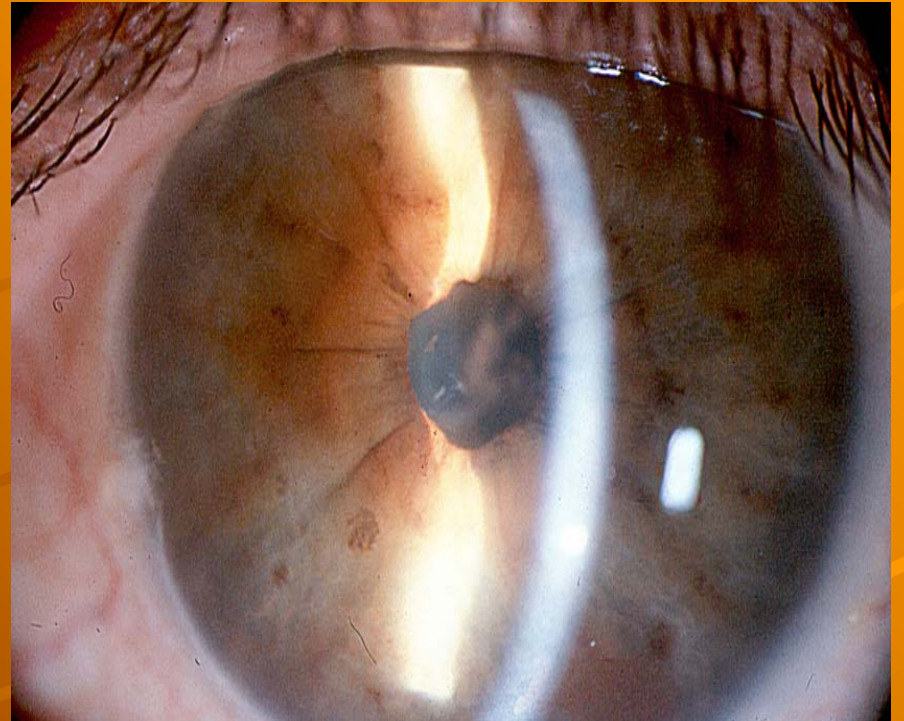
Vogt-Koyanagi-Harada (VKH) Syndrome

- ◆ SNHL, vestibular signs, uveitis
- ◆ periorbital hair loss, depigmentation
- ◆ aseptic meningitis
- ◆ ?autoimmunity to melanocytes



Cogan's Syndrome

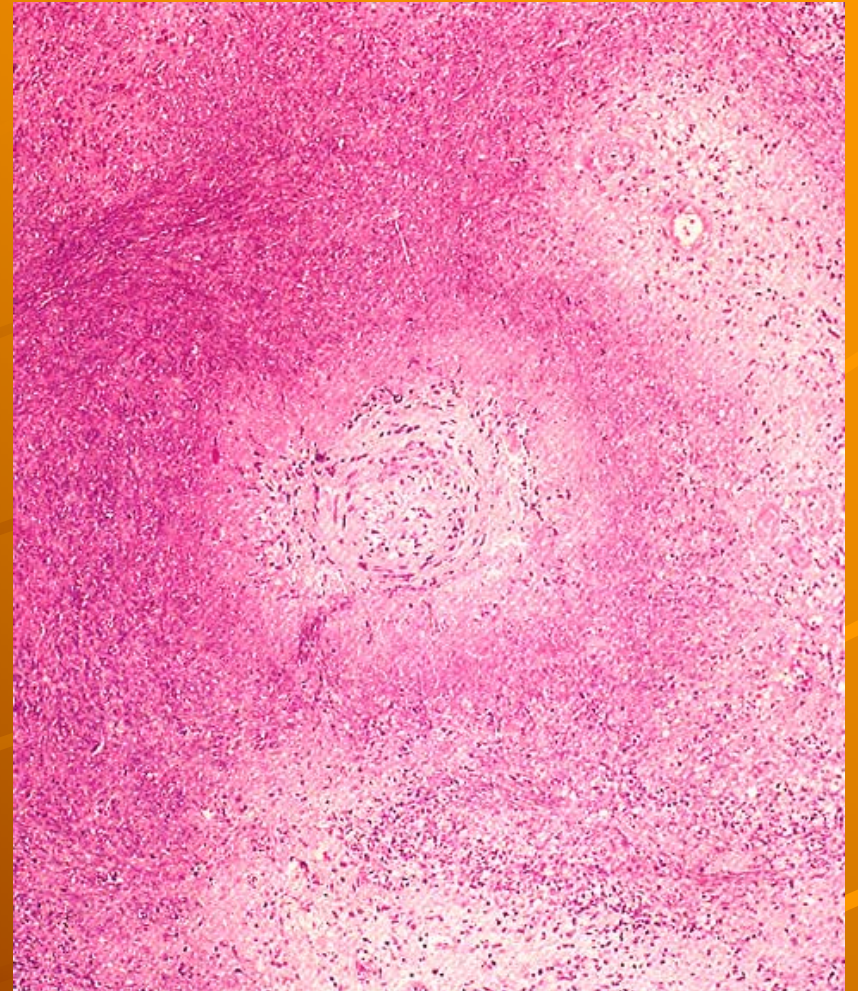
- vertigo, tinnitus, SNHL
- Interstitial keratitis
- -ve FT-ABS



Wegener's Granulomatosis

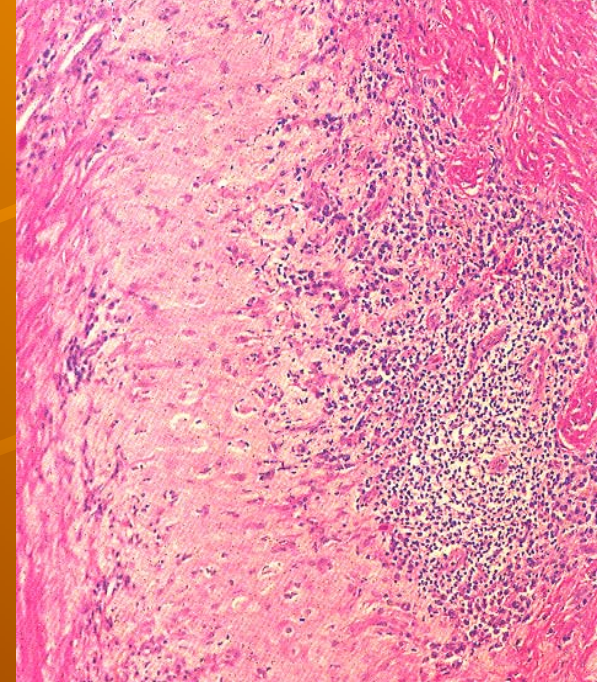
- ◆ Respiratory tract and kidneys
- ◆ 75% SNHL
- ◆ serous OM
- ◆ cANCA 90% specific
- ◆ Vasculitis
- ◆ Hypersensitivity

Type ?



Relapsing Polychondritis

- ✦ Recurrent inflammation of ear, nose, trachea, larynx
- ✦ autoantibodies to cartilage II & IX
- ✦ NSAIDs, steroids, dapsons
- ✦ F +ve VDRL



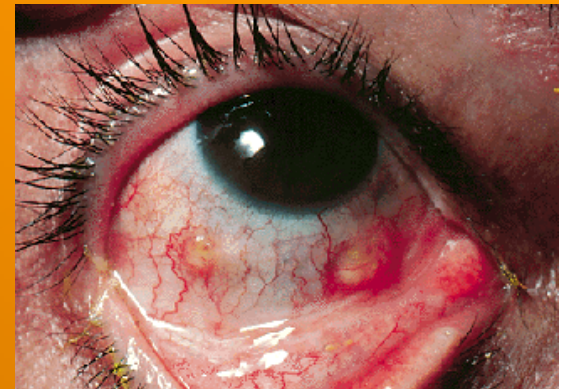
Systemic Lupus Erythematosus

- Anti-nuclear, anti-DNA antibodies
- numerous systemic manifestations
- Vasculitis
- Ear
 - COM
 - SNHL
 - Dysequilibrium
 - (?Ototoxic Rx, Renal failure)



Rheumatoid Arthritis

- Small joints of hands and feet
- Vasculitis
- muscle atrophy
- subcutaneous nodules
- splenomegaly
- IgM 19S and 7S, IgG 7S
75%
- 44% bilateral SNHL
- 75% +ve RF (F+ve>65Y)



Churg-Strauss Syndrome

- ✦ "allergic angiitis granulomatosis"
- ✦ variant of polyarteritis nodosa with systemic vasculitis, asthma, tissue eosinophilia
- ✦ lungs are always involved
- ✦ 70% of patients with nasal obstruction and rhinorrhea



Kawasaki Disease

- "mucocutaneous lymph node syndrome"
- pediatric age group
- fever, conjunctivitis, red and dry lips, erythema of the oral mucosa, rash, desquamation of the fingers and toes, cervical LN.
- 1-2% mortality due to cardiac abnormalities

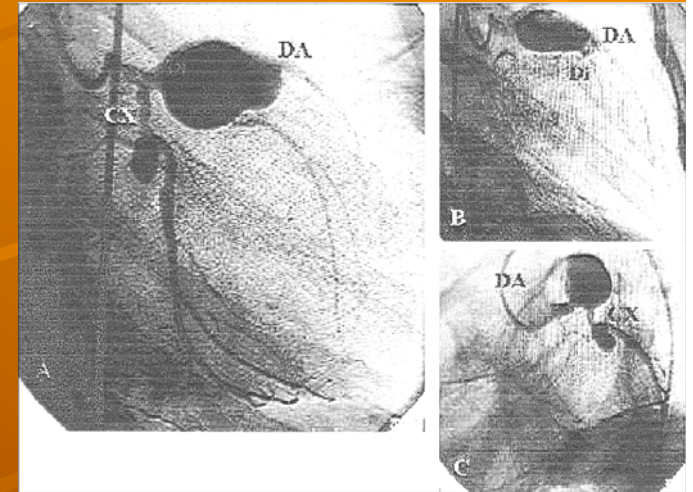
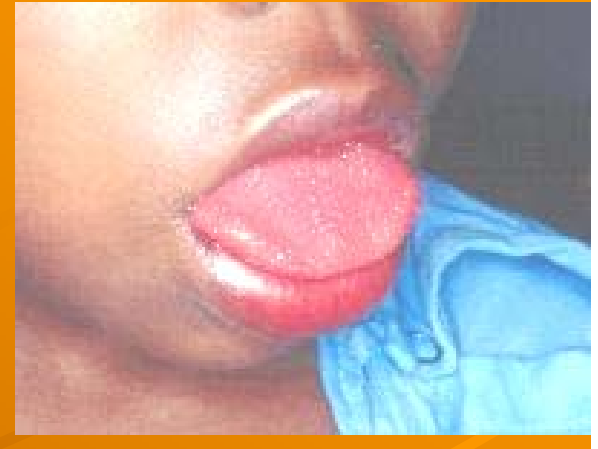
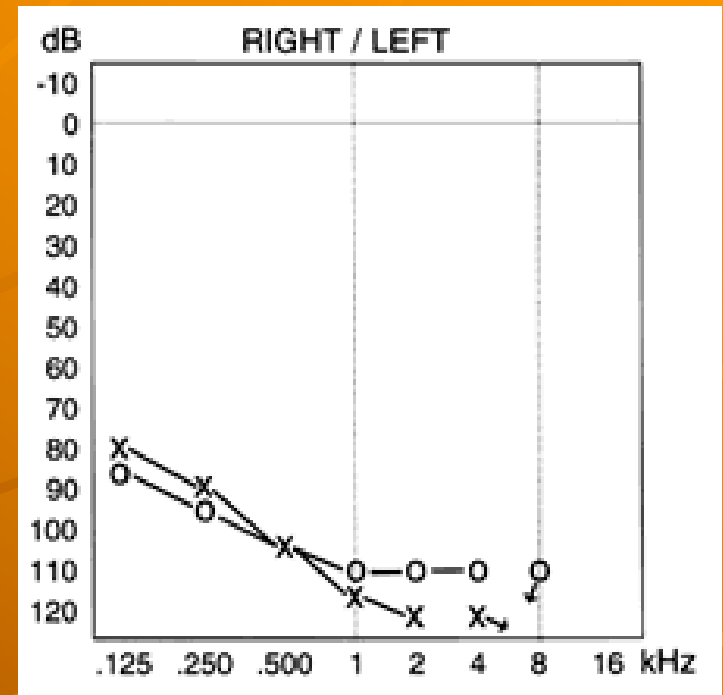


Fig. 3. Coronary angiography performed 80 days after anti-inflammatory treatment showed a significant intimal thickening in the coronary arteries (CN) distal DA and proximal part of the anterior interventricular (DA) arteries, in right (A, B) and left (C) anterior oblique views. A residual giant aneurysm persisted at the beginning of the anterior interventricular artery, though smaller than the one previously observed.

Meniere's Disease

- ✦ ? Autoimmune etiology
- ✦ ? Response to immunotherapy
- ✦ ? 30% with anti-68kDa antibody



Autoimmune basis for Meniere's

Should be suspected

- ◆ Bilateral involvement (1 Dead ear)
- ◆ Thresholds < 50 db
- ◆ Poorer-than-expected discrimination
- ◆ Atypical vertigo



Contralateral Delayed Endo-Lymphatic Hydrop CDEH

- ✦ Inner ear proteins recognized as foreign or non-self
 - Primary process
 - Secondary to trauma or inflammation
- ✦ Some clinicians doubt the existence of the disease
 - Inner ear antigens not yet known
 - Inability to evaluate histopathology

Objectives

- ◆ Cases
- ◆ Physiology of inner ear immune function
- ◆ Autoimmune inner ear disorders
- ◆ Diagnosis
- ◆ Treatment

Clinical Picture

- ◆ Middle-aged women
- ◆ 79% Bilateral SNHL
- ◆ Progressive, *weeks to months* ?SSNHL
- ◆ 75% vestibular symptoms
- ◆ Dizziness, aural fullness ?Menieres
- ◆ 29% systemic autoimmune disease

History

- ◆ Time course
- ◆ Associated symptoms
 - Vertigo/dizziness
 - Aural fullness
 - Tinnitus
- ◆ Ototoxic drug use
- ◆ Symptoms of URTIs
- ◆ H/O head trauma, straining, sneezing, nose blowing, intense noise exposure
- ◆ H/O flying or SCUBA diving

History

✦ PMH:

- Autoimmune disorders
- Vascular disease
- Malignancies
- Neurologic conditions
- Hypercoagulable states
- ✦ Sickle cell disease (African Americans)

✦ PSH: stapedectomy or other otologic surgeries

Physical Exam

- ◆ Complete body exam

 - Rash

 - Joints

- ◆ Ears

- ◆ Neurologic exam – cerebellar findings



Diagnostic Testing

Laboratory testing

- ✦ CBC
- ✦ ESR, CRP
- ✦ Chemistry
- ✦ Cholesterol/triglycerides
- ✦ T3/T4, TSH
- ✦ RPR, VDRL
- ✦ HIV
- ✦ Lyme titer
- ✦ Antigen-specific cellular immune tests
 - Lymphocyte transformation test (LTT)
 - Western blot (hsp70)

Diagnostic Testing

Audiogram – diagnostic and prognostic

- ◆ Pure tone
- ◆ Speech discrimination
- ◆ Tympanometry
- ◆ Stapedial reflex

MRI to rule out CPA tumors

Objectives

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◆ Treatment

Treatment

- ◆ **Steroids (Dx & Rx)**

- Pred 1mg/kg/day for 1 month
- Respond 1 month
- ? Mineralocorticoid (IT Cortisol vs Decadron)

- ◆ **Cyclophosphamide !SE**

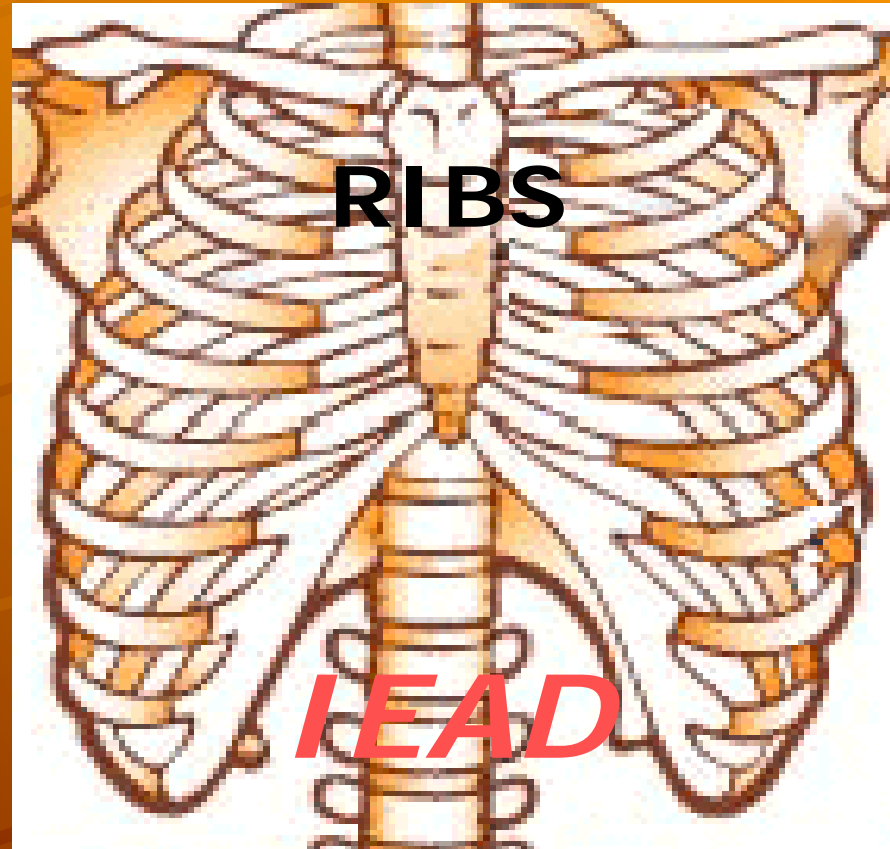
- ◆ **Plasmapheresis**

- ◆ **Methotrexate ?effective**

- ◆ **Cochlear implant**

Conclusion

1. Rapidly progressive (weeks to months)
2. Idiopathic
3. Bilateral SNHL
4. Steroid response



Conclusion

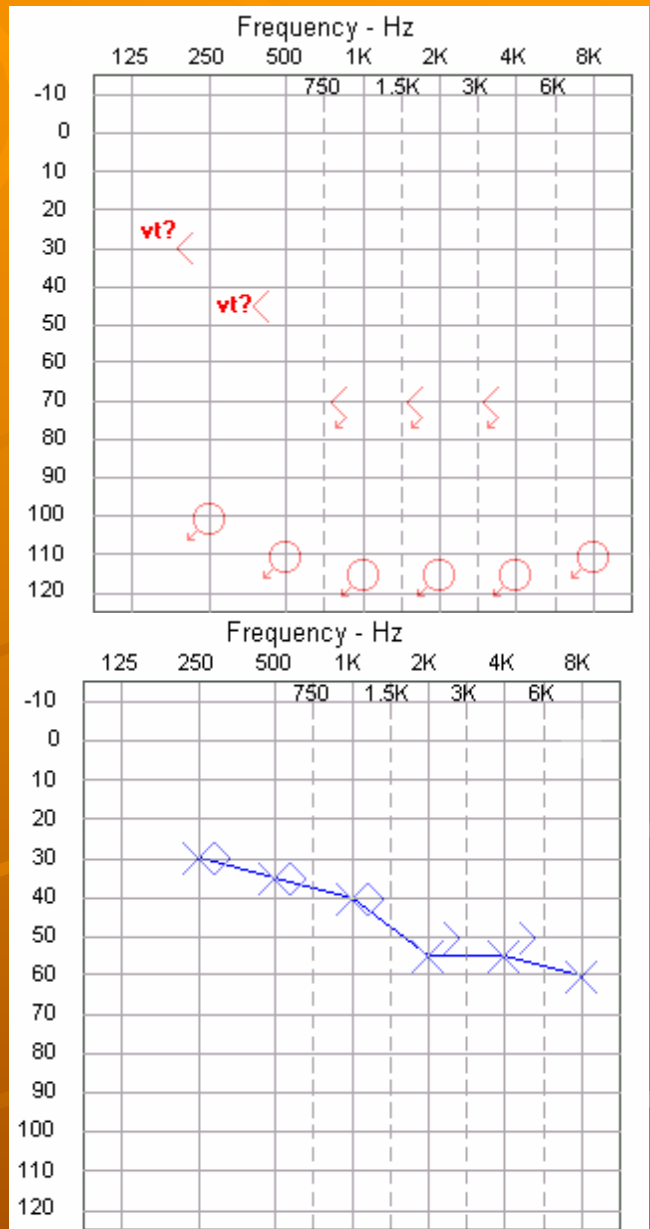
- ◆ Important for physicians to understand the concept of the disease
- ◆ **Treatable** cause of SNHL
- ◆ Treatment must be started early in the disease course
- ◆ Treat with steroids first
- ◆ +/- cytotoxic drugs



Contralateral Delayed Endo-Lymphatic Hydrop CDEH

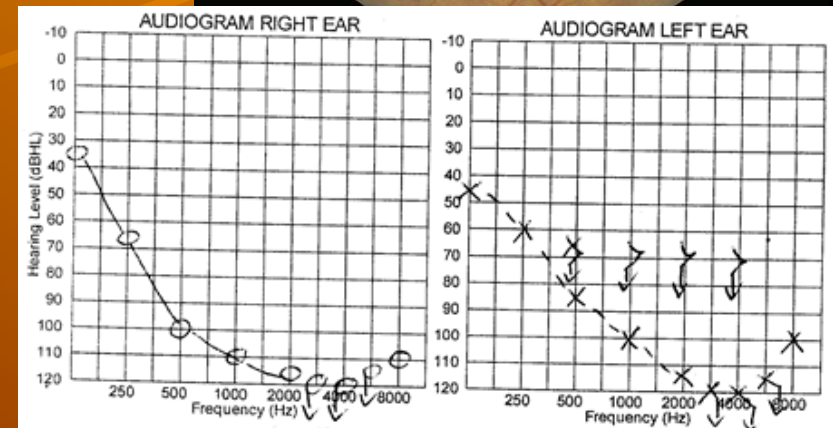
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 - Vertigo

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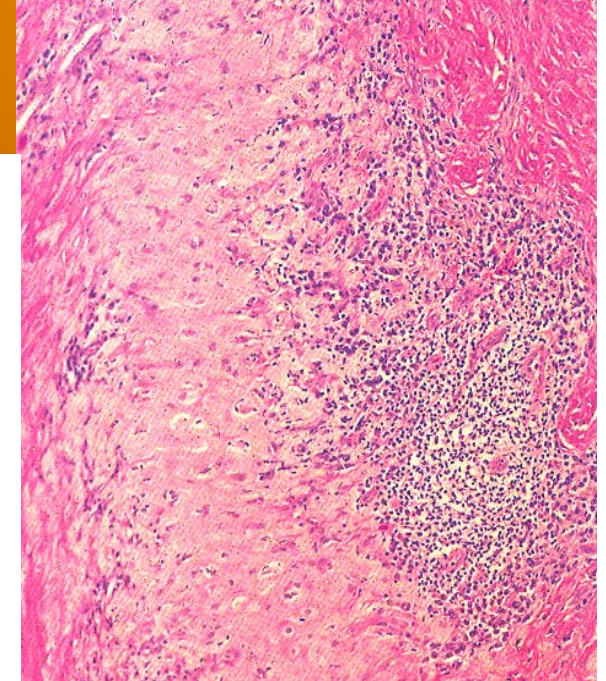
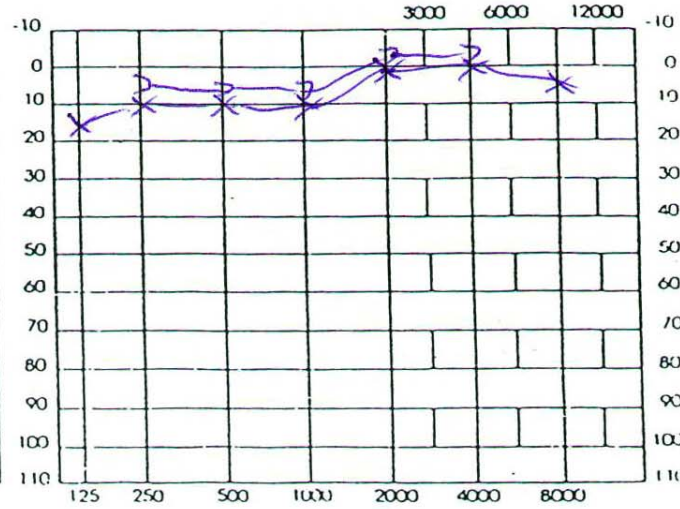
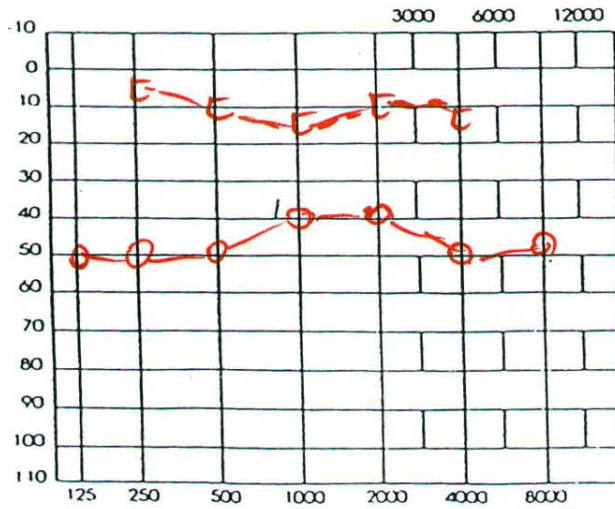
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- ◆ 30 y female
- ◆ SNHL
- ◆ Vertigo
- ◆ Visual loss
- ◆ Morning headache
- ◆ Projectile vomiting
- ◆ CSF: High WBS
-ve culture



Relapsing Polychondritis

- ✦ 30 y male
- ✦ Nose deformity
- ✦ Bi-phasic Stridor
- ✦ Bil fluct- SNHL
- ✦ Rec ear swelling
- ✦ Persistent Rt HL
- ✦ +ve VDRL -ve FT-ABS



Kawasaki Disease

- ◆ 4 y boy
- ◆ HL
- ◆ Fever
- ◆ Rash
- ◆ Cervical lymphadenopathy
- ◆ Chest pain
- ◆ Died in ICU



Thank



You