

CASE FOR DISCUSSION FROM UNIT 2

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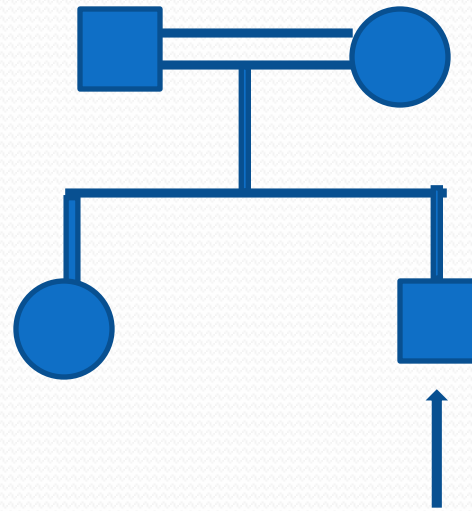
- 9 years boy –Rajesh resident of Mancherial brought by mother with
- c/o loose motions 10-15 episodes a/w mucus & blood,vomitings –non bilious, vomits as and when he feeds since 1 wk
- Low grade fever since 1 wk
- **H/o present illness**
- Acc to h/o child was apparently asymptomatic til 4 months of age when he developed cough,cold,SOB,fever-admitted for 1 month & treated for LRTI.
- h/o repeated LRTI since then-avg 1 /month

- h/o repeated gi infections a/w loose stools a/w blood & vomitings since 1 yr of age-avg 1/month
- h/o recurrent abscesses over skin & scalp, dermatitis,,itching f/b patchy hypo & hyperpigmentation of skin.
- h/o recurrent ear discharge-serous f/b purulent bilaterally since 2yr of age
- h/o repeated infections of eyelids since 2 yr of age
- h/o swelling over the nape of neck-painless static in size –FNAC & Biopsy done at KASTURBA HOSPITAL-SEVAGRAM, WARDHA.reported to be suppurative adenopathy.biopsy report-not found

- h/o decreased appetite not gaining weight since the age of 3 yrs
- h/o white patch over the tongue & oral mucosa extending posteriorly since 1 month
- h/o hematemesis & bleeding per rectum 1 month back for 2 days for which transfusion was done
- h/o pedal edema 1 month back-pitting type now subsided
- h/o 1 admission for pedal edema & loose motions 10 months back for which FFP was transfused.
- h/o 2unit PRP,2 unit FFP,1 whole blood transfusion done.
- No h/o TB contact/similar complaints in family.

- Birth h/o –

born of consanguinous
2nd in birth order,
LSCS, birth wt-3kg.
no h/o neonatal admissions



- **Nutrition history** - EBF til 5 months, complementary feeding at the age of 6 months with mashed rice mixed with pulses and cerelac 3/day
- Calorie deficit-700kcal
- Protein deficit-15g
- Immunisation h/o-BCG,DPT,OPV,HepB 3 doses given
- Developmental h/o-normal
- Family & Socioeconomic h/o – 3rd degree consanguinity, 2nd in order, lower middle class.

● GENERAL EXAMINATION

- Child is sick looking, emaciated, well oriented
- No pallor, icterus, cyanosis, lymphadenopathy, pedal edema
- Vital data
- Pulse-100/mt-regular normal volume, all peripheral pulses felt
- BP – 90/60 mm of Hg lt arm supine
- RR- 30/mt regular
- Temp – 98.3F

- **HEAD TO TOE**-hollowing of cheeks, hypopigmented skin beside ala nasi, forehead,
- Healing ulcer over the rt forearm, dry scaly skin, angular stomatitis,
- Oral candidiasis
- **ANTHROPOMETRY-**

	OBSERVED	EXPECTED	AGE
HC	47cm	52cm	1yr
Ht	100cm	131cm	4yr
Wt	11kg	29kg	1.5yr















- **SYSTEMIC EXAMINATION**

- CVS- normal

- RS – normal

- CNS – normal

- GIT – oral candidiasis extending over post pharyngeal wall

- Palpation-P/A-soft,no organomegaly

SUMMARY

- 9y male child born to consanguineous marriage with h/o
repeated respiratory tract infections since 4m of age, recurrent G.I. **infections** since 1yr of age, **recurrent skin infections**, since 2yr of age, with **hematemesis & lower gi bleed** with transfusion of blood products.



Case open for discussion

Probable diagnoses

1. **Wiskott aldrich syndrome**
2. Chronic granulomatous disease
3. Acquired immunodeficiency

INVESTIGATIONS

- **CBP**
- 17/8 – Hb-10.6g%, platelets-40,000/cumm
- 23/8- Hb-10.6g%, platelets – 20,000/cumm
- 28/8 – Hb-9.8g%,platelets – 90,000/cumm
- 17/9 – Hb-13g%,platelets - >3lakh/cumm,NC/NC
- **18/9 – micro platelets-tiny sluggish scattered platelets seen**
- WBC-14000cells/cu mm(N-59%,L-35%,M-4%,E-2%)
- Blood picture – normo cytic normo chromic

- **PT-35.9sec(13.4 sec)**
- **APTT – 36.7sec(30sec)**
- Total proteins-5.9(albumin-1.9,globulin-4.0)
- LFT - normal
- Serumelectrolytes – normal
- **HIV1&2 – NEGATIVE**
- **Mx – nonreactive**
- CXR – normal
- ESR – 10mm-1sthr,12mm-2ndhr
- Stoolc/s – no pathogenic organisms grown
- USG abdomen – coarsened echotexture of liver,periportal fibrosis,minimal free fluid in abdomen
- **NBT dye test – normal range**
- **IgA,IgM,IgG – normal level**
- **WASP gene analysis report awaited**

Wiskott aldrich syndrome

- X linked recessive condition
- **Triad – immunodeficiency ,micro platelet thrombocytopenia, eczema**
- Result from mutation of gene encoding WASP at X11p
- WASP- protein involved in the rearrangement of actin & important in interactions b/w T lymphocytes &APC
- It also affects the cytoskeleton of platelets & is involved in signal transduction.

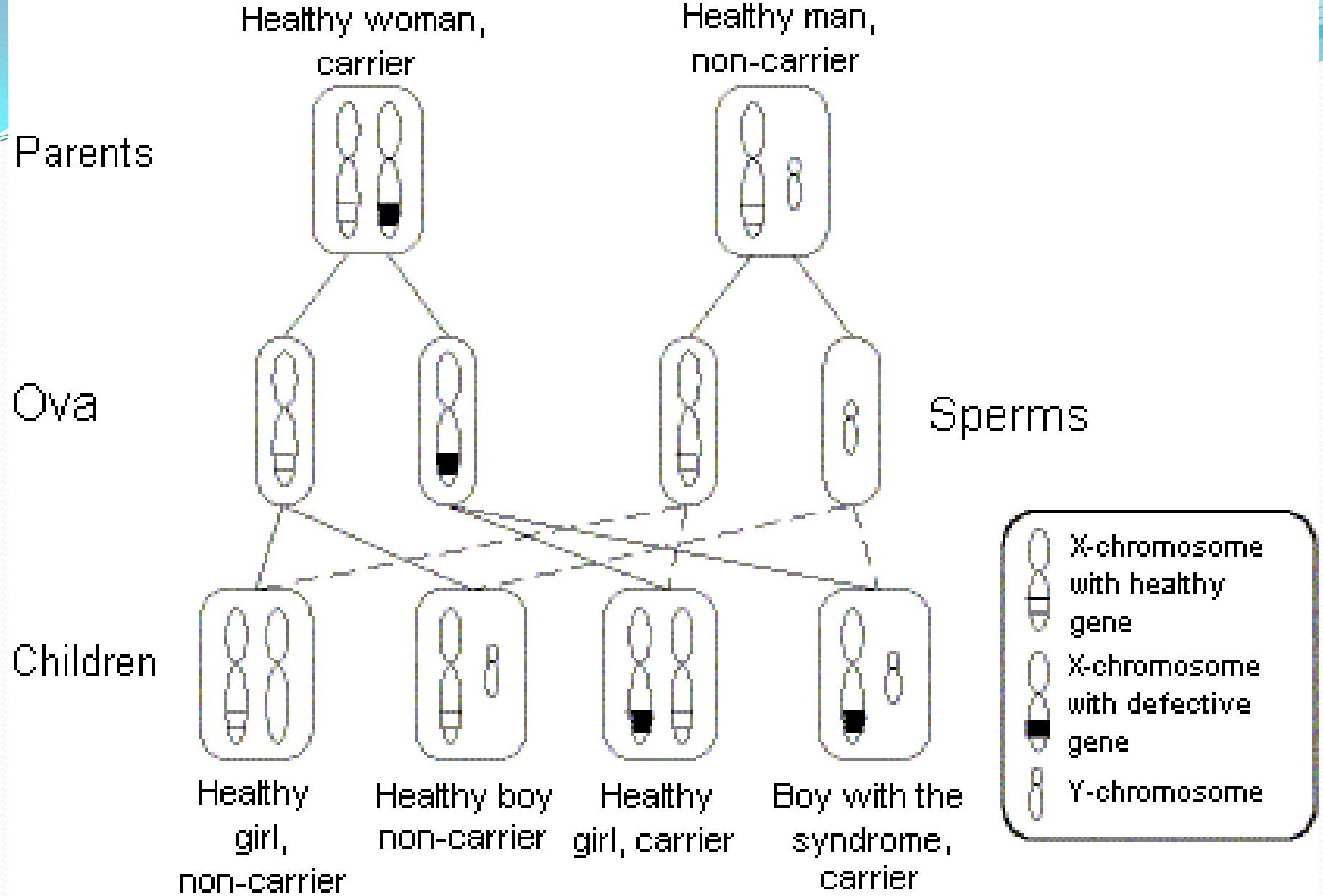


Figure: X-linked recessive genetic trait from a healthy woman who is a carrier

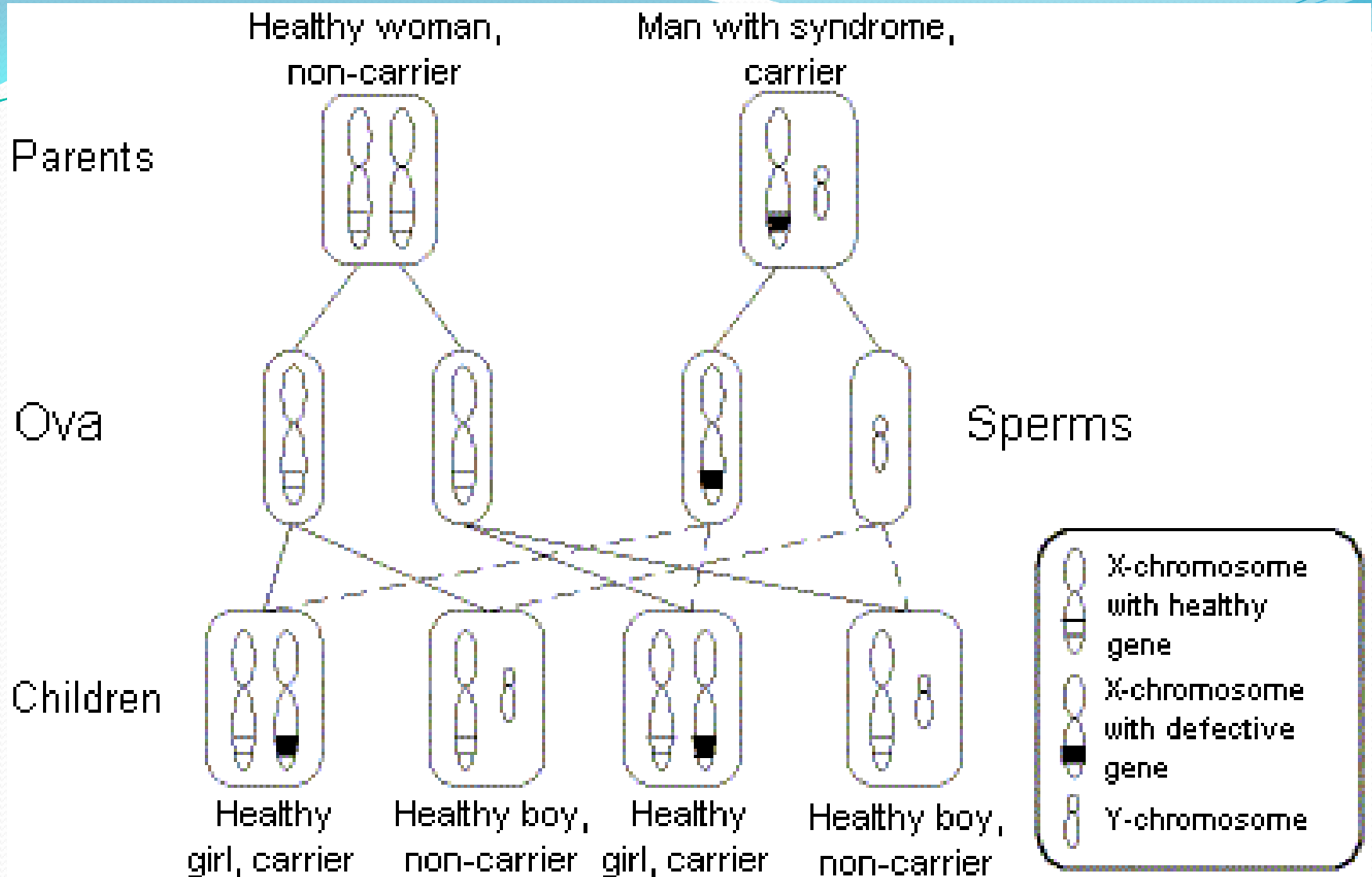
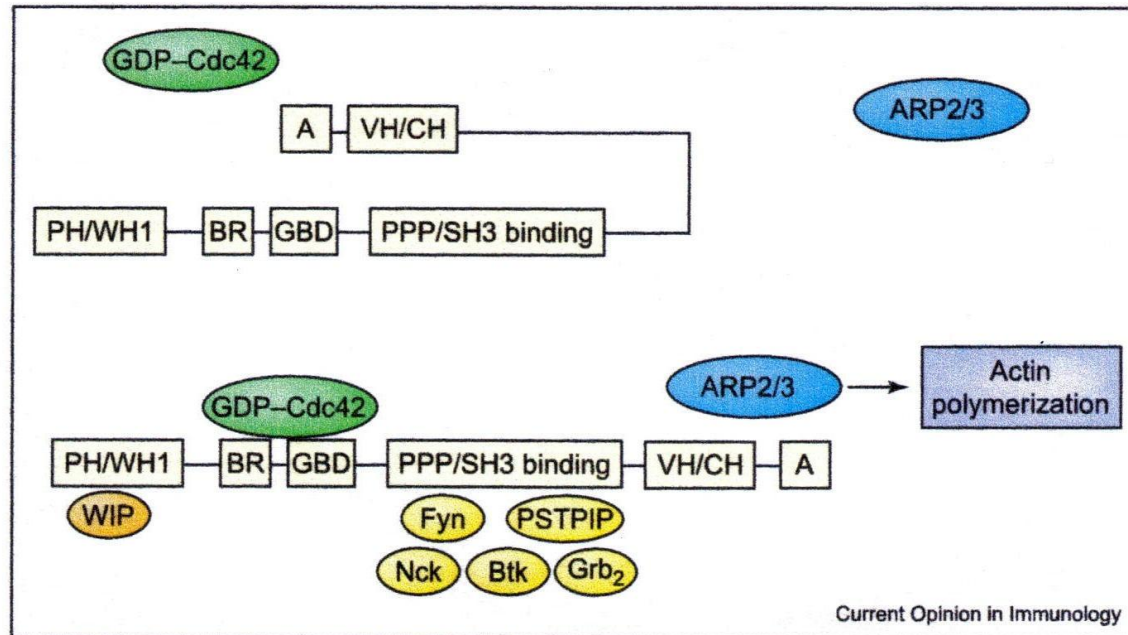


Figure: X-linked recessive genetic trait from a man with the syndrome who is a carrier

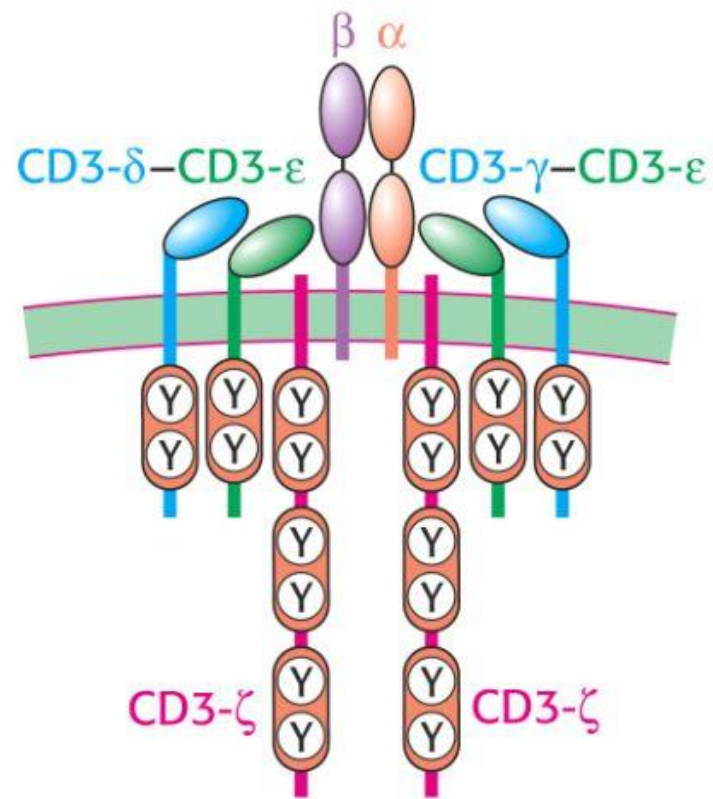
ACTIN REORGANISATION

- WASP is involved in the reorganization of the actin skeleton. When the WAS protein is altered, it does not properly bind and actin reorganization is prohibited.



EFFECT ON T LYMPHOCYTES

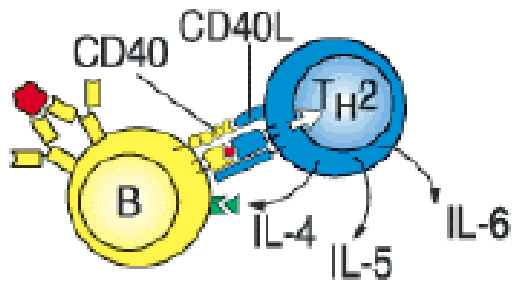
- Cytoskeleton reorganization is involved in the binding of T lymphocytes to antigen-presenting cells through CD3 cross linking.
- Without actin reorganization, CD3 is not properly presented at the cells surface and the T cell is not activated.
- Causes recurrent viral and fungal infections (as noted in symptoms).



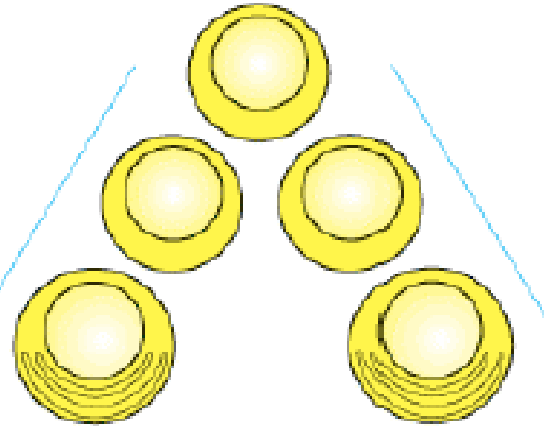
EFFECT ON B-LYMPHOCYTES

- Thymus dependent B lymphocytes need T cells for activation and differentiation.
- B cells only able to produce IgM through thymus independent B lymphocytes.
- Causes recurrent bacterial infections because proper antibodies are not produced against certain bacteria.

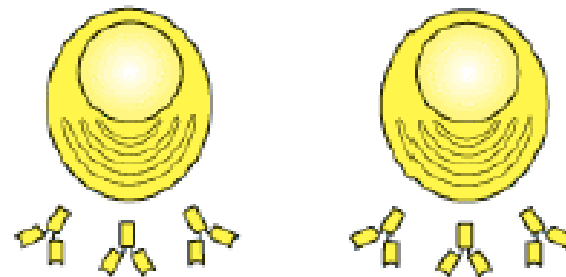
Antigen recognition induces expression of effector molecules by the T cell, which activates the B cell



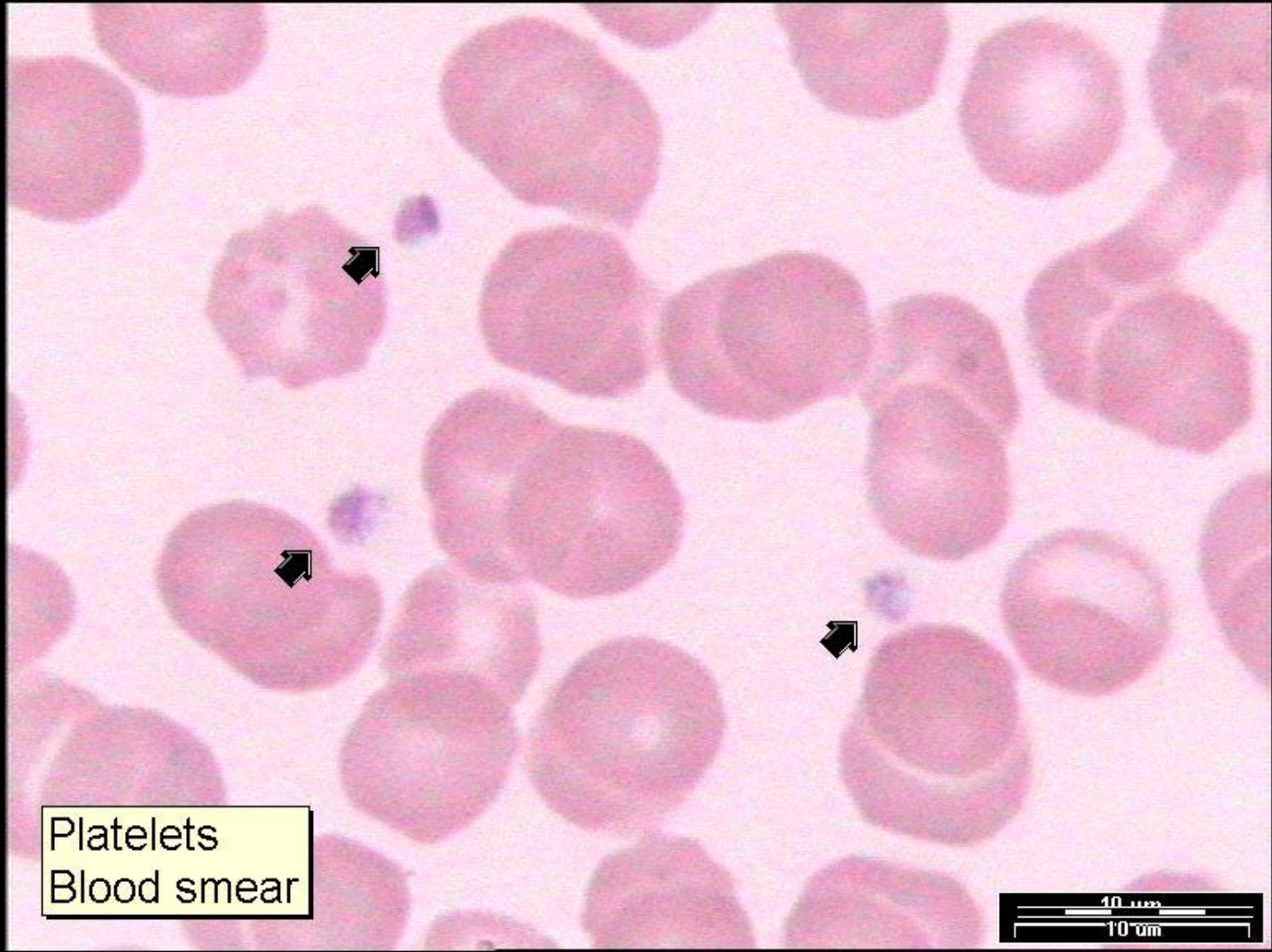
B-cell proliferation



Differentiation to antibody-secreting plasma cells



of
er
cell



Platelets
Blood smear



May-Grunewald Giemsa X1000

Symptoms

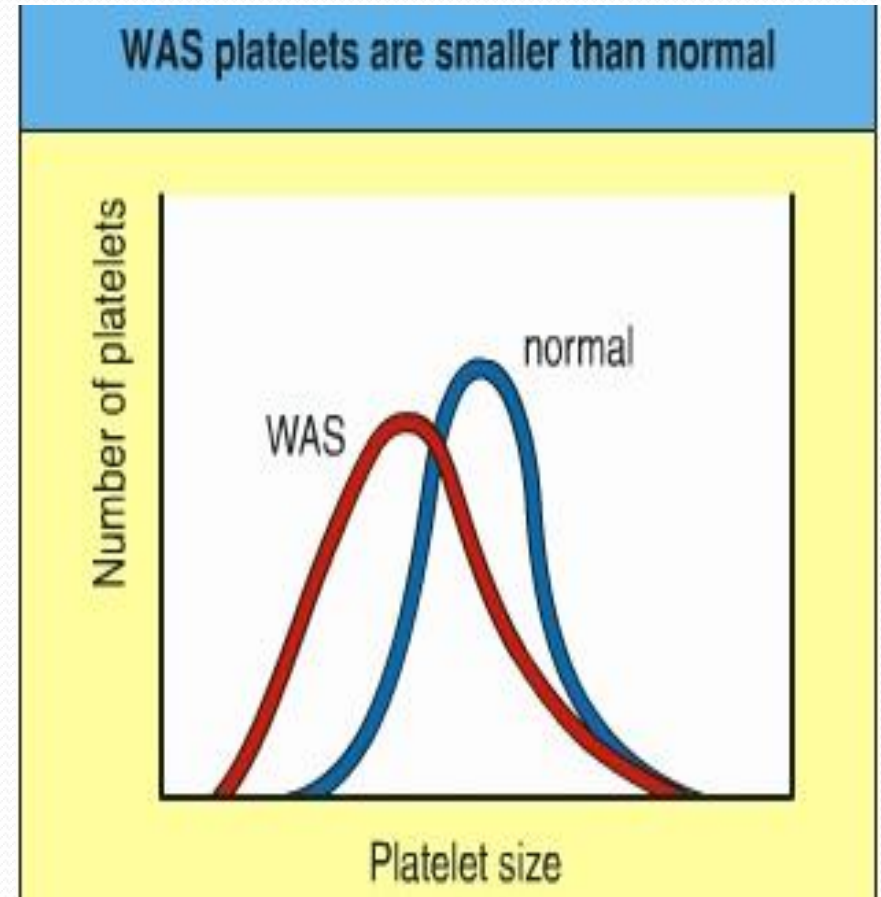
- **Thrombocytopenia**
(low platelet count and disturbed platelet function)
- **Recurrent infections**
- **Eczema**
- Malignancies in the form of leukemia and lymphoma occur in more severe cases



- Prolonged bleeding from the circumcision site or bloody diarrhea during infancy.
- **Atopic dermatitis & recurrent infections-1st yr of life**
- **Strep pneumonia influenza having polysaccharide capsules cause otitis media, pneumonia, meningitis & sepsis.**
- Later infections with pneumocystis carinii & herpes become more frequent.
- Survival beyond teens is rare
- Infections, bleeding & EBV associated malignancies are major cause of death.

INVESTIGATIONS

- a. Size of platelets
- b. Antibody responses after immunization-ELISA
- c. Highly variable pattern of Igs & albumin.
- d. Predominant pattern- low IgM, high IgA&E, normal /low IgG.
- e. WASP gene analysis



Treatment

1. Good supportive care, nutrition, Mx of eczema & skin infections, use of killed vaccines.
2. Infection prophylaxis with antibiotics.
3. Platelet transfusions
4. Splenectomy & high dose IVIG with systemic steroids for autoimmune complications.
5. Monthly infusions of IVIG regardless of serum levels.
6. **BMT & cord blood transplantation-treatment of choice.**

CHRONIC GRANULOMATOUS DISEASE

- Characterized by the ability of neutrophils & monocytes to ingest but their inability to kill catalase positive micro organisms because of defect in the generation of microbial oxygen metabolites.
- X linked recessive condition, auto recessive also seen
- NADPH oxidase defect.
- Recurrent infections of skin, lung, liver with catalase positive bacteria, fungi with subsequent granuloma formation.
- Diagnosis – NBT dye test
- Treatment-stem cell transplant, granulocyte infusions, IF-gamma

10 warning signs of immunodeficiency

1. 8 or more new **ear infections**/yr.
2. 2 or more sinus infections/yr.
3. **2 or more months on antibiotics** with little effect.
4. 2 or more **pneumonias**/yr.
5. Failure of an infant to **gain weight/grow normally**.
6. **Recurrent deep skin or organ abscesses**.
7. **Persistent thrush in mouth** or elsewhere on skin after 1yr
8. **Need for iv antibiotics to clear infections**.
9. 2/more deep seated infections.
10. Family h/o immunodeficiency.

characteristics	Combined deficiency(T& B cell)	Ab deficiency(B cell)	Phagocyte defect	Complement defect
Age of onset	Early,before 6 months	After 3-6 months	Early onset	Any age
Specific pathogens	pneumo,H influ,pseudomonas:CMV,EBV:Candida,aspergillus:pneumocysti	Pneumo,H influ: enterovirus :giardia	Staph aureus,serratia,nocardia,candida,aspergillus	Meningococci.pneumo,H influ,
Affected organs	FTT,meningitis,septicemia,sino pulm,protracted diarrhea,recurrent candidiasis	Recurrent sinopulm,meningitis,chronic malabsorbtn,arthritis	Dermatitis,impetigo,osteomyelitis,periodontitis,pneumonia,abscesses,adenitis	Meningitis,septicemia,recurrent sino pulm
Special features	GVHD,disseminated BCG,polio.absent thymic shadow	Autoimmunity,lymphoreticular malignancy,chronic enteroviral encephalitis	Poor wound healing,	SLE,vasculitis,DM,angioedema,Glomerulonephritis

Take home message

1. Too many infections consider warning signs.
2. Rule out common causes first.(HIV,TB,foreign body)
3. Take good h/o,-
location,organism,frequency,response to
treatment,hospitalisation,family h/o.
4. Order simple tests CBC,differential,quantitative Ig
assay related to age.
5. Categorise the patient and order screening tests
accordingly.



Thank you