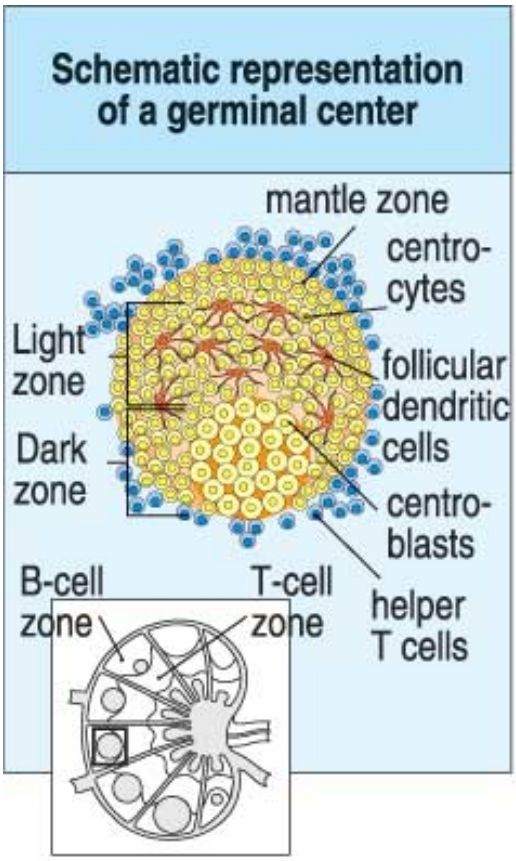
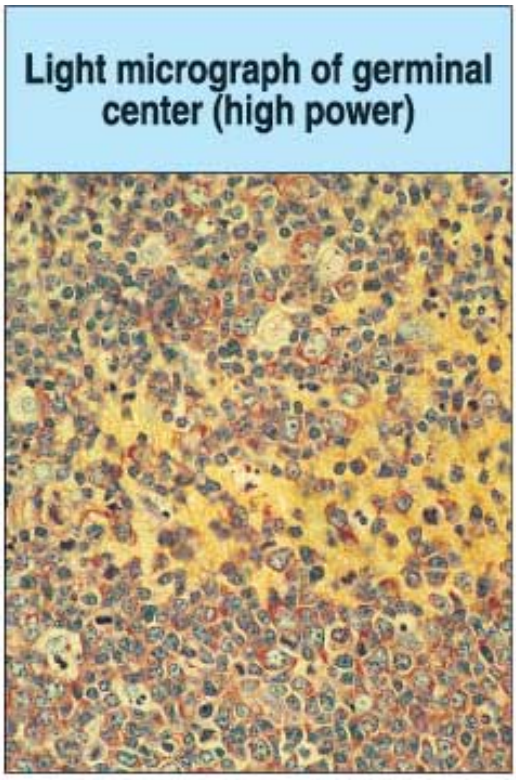
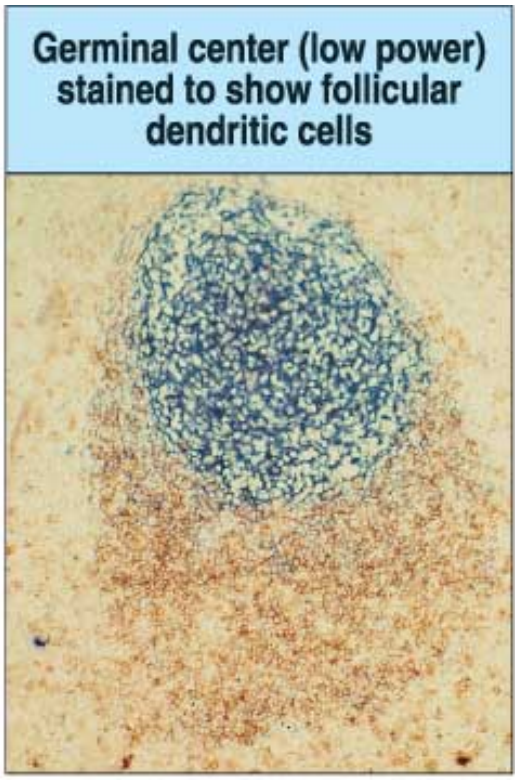
Lecture 7.
Learning Objectives and Summary







7. Regulation of B cell development and the humoral response

Learning Objectives

1. Learn when, where and how the antigen-independent, primary B cell repertoire is established.
2. Learn how central tolerance is established.
3. Learn when, where and how antigen-dependent B cell responses are generated, especially the nature of T-cell dependent germinal center reactions.
4. Learn how peripheral tolerance is established.
5. Apply this knowledge to understand the pathogenesis of inherited human diseases that result from defects in B-cell development.

SUMMARY

1. Antigen-indpendent B-cell development occurs in the bone marrow: DNA rearrangements create a diverse primary repertoire, pre-BCR and BCR provide developmental checkpoints.

2. Self-reactive clones are edited, deleted or anergized in the bone marrow, providing central tolerance.

3. Antigen-dependent B-cell development occurs in the spleen and lymph nodes: T-dependent responses involve T cells for both cell-cell contact and soluble mediators. T-independent responses involve repeating epitopes and activation of innate immune receptors.

4. Peripheral B-cell tolerance in the spleen occurs by editing, anergy or clonal deletion.

5. Affinity maturation and CSR occur primarily in germinal center B cells and require T cells, follicular dendritic cells and antigen. Memory B cells and Ig-secreting plasma cells emerge from the germinal center reaction.

6. Immune deficiencies result from genetic defects in Bruton's tyrosine kinase (Btk), CD40, CD40L & AID.