

一. 是非題

O 10. IgA-associated components are transported by pIgR secreted from epithelial cells.

IgA1:IgA2=10:1(血液); 3:2(上皮)(因為IgA2不易水解)

polymeric IgA和pIgR結合, 把IgA送入上皮

(O) 1. 抗IgE的抗體可作為抑制過敏的藥物 【CM105】

因IgE和過敏有關, 見PPT14。

(X) 2. Th1 cells release cytokines that result in an increased production of eosinophils and mast cells in the bone marrow. 【96醫學】

因Th1分泌的cytokine是IFN- γ , 會抑制IgE, 抑制過敏反應, 不會導致過敏相關細胞在骨髓中增加製造。(PPT14)

過敏引發Th2 priming Th1&Th2 produce IL-4&IL-13 -> B cell produce IgE -> IgE attach to mast cell

Mast cell: 分泌IL-5, 刺激eosinophil 產生 produce IL-4 and express CD40L -> Th2 activated and B cell activated

(O) 3. Vaccine against H. influenza type B is conjugate of bacterial polysaccharide and tetanus toxoid protein. 【M104】

【CM105】 【M102】 (見ppt13)

Hib vaccine: B recognizes LPS, T recognizes Tetanus toxoid protein

Linked recognition: B認polysaccharide; T認tetanus toxoid protein, 兩種結合一起, 活化T後活化B

(O) 4. The brain is devoid of immunoglobulin.

(X) 5. Centroblasts are the main cell population of the light zone of the germinal center. (ppt21)

Dark Zone-細胞聚集進行複製的位置, 所以顏色較深, 透光率很差。其中, 有較大的細胞為centroblasts, 功能為進行 proliferate Apical light zone(memory&plasma cell), Basal light zone(high-affinity centrocyte), Dark zone(centroblast)

(X) 1. Mismatched blood transfusion will cause type 3 hypersensitivity (type 2) 【CM104】

type 2: ADCC ex. Rh+ baby-新生兒溶血症(Hemolytic disease of fetus & newborn)

(X) 3. The wheal-and-flare reaction is an early phase of type IV hypersensitivity. →應為type I的反應(由IgE結合上過敏原引起 mast cell的活化) 【M103】

(X) 4. Autoimmune hemolytic anemia is mediated by type 3 hypersensitivity. 【M103】

Type 2 過敏反應。有些人會對藥物過敏, 產生anti-drug Abs 會摧毀藥物所結合的細胞。若藥物結合的是紅血球就會造成hemolytic anemia(溶血性貧血)。

type 3: immune complex 的沈積(多自體免疫疾病) ex. rheumatic fever

(X) 1. IFN- γ is a promoter of type I hypersensitivity. 【M104】

☑ IFN- γ 抑制Th2, 而type I hypersensitivity是由Th2與B cell交互作用產生IgE而發生。IFN- γ 屬於type 4

type 4: Th1分泌chemokine, IFN- γ (活化macro.), TNF- α /b(tissue destruction)

IFN- γ promotes epithelial cell express FasL

(X) 2. 記不太清楚, 大意是說Ab-coated pathogens 接上Fc receptor引發的都是activation的反應。 【CM105】

☑ Fc receptor上的domain如果是ITIM的話, 不是activation的反應。 EX: Fc γ R2B2, Fc γ R2B1

(X) 3. Arthus reaction will cause type II hypersensitivity. 【CM105】

解: 應為type III。Arthus reaction為局部的抗原與IgG結合產生免疫複合體(immune complex), 活化補體分子後活化白血球參與發炎反應的現象。Immune complex清除時傷害到自體組織為造成type III hypersensitivity的原因。(詳見第十二次共筆 p.28)

(X) 4. The local inflammatory response of type IV hypersensitivity is called Arthus reaction. 【M102/CM103】

解: 應為type III。Arthus reaction為局部的抗原與IgG結合產生免疫複合體(immune complex), 活化補體分子後活化白血球參與發炎反應的現象。Immune complex清除時傷害到自體組織為造成type III hypersensitivity的原因。(詳見第十二次共筆 p.28)

(X) 7. IgM is superior to IgG in FcR-mediated opsonization.

IgG>IgA(補體活化: IgG, IgM; 中和/擴散到血管外: IgA, IgG)

(X) 8. Babies can acquire IgE-mediated allergies by passive transfer of maternal antibody.

[Babies有兩種保護網: 通過胎盤之IgG、母乳中的IgA]

(X) 9. Neutrophils and mast cells possess high level of Fc ϵ RI.

[Neutrophils don't possess high level of Fc ϵ RI(IgE receptor)]

Fc ϵ RI: affinity高, 多在mast cell/ basophil, type I 過敏主要角色

Fc ϵ RII: affinity低, 在B/T/eosinophil/platelet/FDC, 有proteolytic cleavage site

(X) 11. The degranulation of mast cells can be induced by the intradermal injection of Fab of anti-Fc ϵ RI.

[by the activation of Ag cross-link; anti-Fc ϵ RI blocks the degranulation; mast cell 的FcR 為Fc ϵ RI]

Degranulation happens when Ag exists, with Fc ϵ RI binding, attaching to mast cell

- (O) 12. ADCC is involved into the development of hemolytic anemia.
- (O) 13. Immune complexes can be cleaned in the liver faster than in the kidney.
- (X) 16. FcγRIII has high affinity to IgE. [FcγRIII has high affinity to IgG1, FcεRI has high affinity to IgE]
- (X) 17. The function or activity of NK cells is the most important host defense mechanism against bacterial toxins.
- (O) 18. Thymus-independent Ag can activate B cell, and stimulate the production of IgM.
- (O) 20. Stimulating Ab production can induce ADCC resulting in autoimmune disease.
- (X) 22. LPS is an exotoxin produced by bacteria. [LPS is an endotoxin]
- (X) 23. Ag-Ab complexes can be cleaned off faster in arteries than in the liver. [slower in arteries]
- (X) 24. Attenuated vaccines can be developed for all the pathogenic viruses and bacteria. **TI couldn't**
- (X) 25. Naïve lymphocytes extravasate into lymph node, spleen and Peyer's patches through HEV for antigen-specific activation.
 [1. 只有進入 lymph node 才是透過 HEV, spleen 是透過 marginal sinus, Peyer's patches 非本次範圍。
 2. 另外, B cell 進入 lymph node 和 spleen 是受 chemokine 吸引或隨血液循環進入, 不需 Ag-specific activation]

(O) 4. Rheumatic fever can be caused by the cross-reaction of Streptococcus-induced autoantibody to heart muscle after streptococcal infection

(X) 2. The molecular mimicry can contribute to vaccines against infection

Molecular mimicry 可能使 vaccine 產生 autoimmunity **Pathogen with antigen similar to self-antigen**

X 1. The armed helper T cells express high level of CD40 to stimulate the proliferation and differentiation of B cells. **CD40L**

X 2. Both IgA and poly-Ig receptor are expressed by Ig-A secreting cells. **pIgR is expressed by epithelial cell**

O 6. T cells in lamina propria express high level of α4:β7 integrin.

O 7. Effector T cells express different chemokine receptors for homing to small intestine or colon

(大腸是 CCL28, 小腸是 CCL25)

O 10. IFN-γ is an important mediator for type IV hypersensitivity

X 4. In order to provide efficient help, B cells and helper T cells must recognize same epitope of the same molecular.

X 5. Antigen-binding B cells interact with helper T cells and are trapped in the T-cell zone of the spleen. **B&T cell zone border**

X 7. Most individuals with IgA deficiency are normal and mucosal infections are not more prevalent than usual. **IgA is the first immune defense of the mucosal system**

O 8. Serum sickness is a classic example of a transient immune complex-mediated syndrome. **Type III hypersensitivity**

X 9. The activation of T cells does not play any role in the onset of type I hypersensitivity.

O 10. Immunotherapy with repeated injections of small amount of allergens (hyposensitization) has been known for some time to reduce the severity of type I hypersensitivity.

___ 12. Type IV hypersensitive reaction can be induced by poison oak in sensitive individuals.

二. 選擇題

10. 如果遇到有毒的長春藤 (poison ivy)，會產生皮膚的症狀，則下列敘述何者為非？

- (A) 跟第二型 T 輔助細胞有關 *Type IV hypersensitivity, Langerhan cell express Ag to Th1 -> activate*
(B) 跟長春藤葉子上的脂溶性物質有關 *keratinocyte -> attracting more non-specific T cell*
(C) 通過皮膚的物質會被蘭氏細胞 (Langerhan's cells) 所攝取
(D) 可能導致皮膚產生水泡

1. Which is not TI-2 antigen? 【M103】

- (A) Polysaccharide (B) LPS (C) dextran (D) poly amino acid

LPS is TI-1

ANS: (B) LPS是TI-1 (C) dextran為一種葡萄糖聚糖

TI-1: LPS

TI-2: polysaccharide, dextran, Poly-D amino acid (是一種Polypeptide capsule的結構)

TD: ovalbumin

(參考資料: PPT8,9, http://big5.wiki8.com/kangyuan_103669/)

2. Which of the followings is NOT T-independent antigen? 【M102】

ovalbumin is TD

- (A) dextran (B) LPS (C) Poly-D amino acid (D) ovalbumin

ANS: (D) ovalbumin 卵清蛋白為一種可溶性蛋白質，應是TD。

3. IL-4 stimulates the production of (A) IgE (B) IgG2a (C) IgG3 (D) IgM

(1%, 參考94醫師國考) 【96醫學】(PPT14) *Th1&Th2 produce IL-4&IL-13 -> B cell produce IgE -> IgE attach to mast cell*

Ans: (A)

produce IL-4 and express CD40L -> more Th2 and B cell activated

4. Which cytokine induces B cells to undergo class switch to IgE?

- (A) IL-2 (B) IL-4 (C) IL-5 (D) IL-10 【95中醫】(PPT14) *Th1&Th2 produce IL-4&IL-13 -> B cell produce IgE -> IgE attach to*

Ans: (B)

mast cell produce IL-4 and express CD40L -> more Th2 and B cell

5. Which molecule is important to carry IgG across placenta?

- (A) CR1 (B) C1q (C) FcR1 (D) FcRn

Ans: (D) 參見【PPT29】共筆p.17

6. Which of the following molecule is important in the clearance of immune complex in circulation?

- (A) CR1 (B) CR2 (C) C3a (D) C4a *Ag-Ab complex binds C1q&C3b -> bind to CR1 through Ab -> brought to liver clear*

Ans: (A)

過多的的抗體抗原複合物，一定要被清除，不然會引起過敏反應。其會先和C1q結合，再結合上C3b，接著透過抗體和紅血球上的 complement receptor(CR1)結合，並帶到肝、脾代謝 共筆11p19

1. Which of the following lymphoid tissue is not organized lymphoid tissue? 【M103】

- (A) isolated lymphoid tissue (B) lamina propria (C) Peyer's patch (D) palatine tonsil

Ans: (B) ,

organized lymphoid tissue會聚集成一區域，且有膜包著的構造，lamina propria為分散在腸道內，組織時有學到，他們又稱diffused lymphoid organ

2. Which of the following lymphoid tissue is not part of the Waldeyer's ring? 【CM103&M102】

- (A) Adenoid (B) Lingual tonsil (C) Peyer's patch (D) Palatine tonsil

Ans: (C) ,

看CH12 伍、Waldeyer's ring，口腔中的才是

3. 以下哪個不是Salmonella 侵入腸細胞內的方式? 【CM104】

- (A) 直接穿過或毀壞M cell (B) 利用DC的長dendrite入侵 (C) 直接從basal面進入腸細胞
(D) 從lumen面利用鞭毛侵入

Ans: (C)

(1) Salmonella透過M cell進入人體被macrophage吃掉後，macrophage藉由IL-12和IL-18的分泌啟動Th1的活化路徑，同時macrophage也會分泌IFN γ 。另外，菌上的鞭毛也會被TLR-5辨識。

(2) Salmonella直接利用fimbriae進入上皮細胞。

(3) DC伸出觸手(dendrite)穿過上皮細胞直接將細菌吞進肚子裡。

4. which of the following mutated gene is associated with crohn's disease? 【M103】

- (A) NOD2 (B) FasL (C) TNF-alpha (D) TNFR 1

NOD2 defection causes crohn's disease(inflammatory bowel disease)

Ans : (A) , 看CH12貳拾貳、Commensal bacteria can prevent inflammatory responses in the intestine

若以上的機制失常的話(例如NOD2失常),會造成inflammatory bowel disease(Crohn's disease)

5.the wrong features of a potential allergen 【CM105】

(A)has protease activity (B)high solubility (C)stable (D)large molecular weight

Ans : (D)

6.下列何者為possible allergens的特性? 【CM103】

(A) easy to be degraded (B) protease activity (C) large molecular weight (D) not soluble

Ans : (B)

7. Which of the following is not the risk factor for asthma? 【M102&CM103】

(A) have a SNP (single nucleotide polymorphism) linked to IRF (interferon regulatory factor) gene

(B) be the first child in a family

(C) be infected with intracellular bacteria

(D) live in a rural area

Ans: ? ?

較容易患過敏的因素有：

1.越是西方化乾淨的環境越容易發生過敏疾病

2.在家裡排行前面的(老大老二老三)較容易發生過敏，排行小的(老四老五)較不易過敏

3.家裡有養狗當寵物較不易過敏

(A) 單核苷酸多型性 (Single Nucleotide Polymorphism, 簡稱SNP) 指的是DNA序列上發生的單個核苷酸鹼基之間的變異。而Interferon Regulatory Factor(IRF) Family, 屬於一種干擾素轉錄调控因子, 此因子利用JAK-STAT訊息傳遞路徑(signaling pathway)调控干擾素的生理功能。老師說就是降低Interferon γ (IFN- γ)的東西。而TH1會分泌IFN- γ 來抑制TH2分泌IL-4,IL-13活化b cell及IgE的分化, IFN- γ 降低則IgE分化提高, 過敏反應增加。

總之, have a SNP (single nucleotide polymorphism) linked to IRF (interferon regulatory factor) gene→就是IRF基因突變→無法降低IFN- γ →IFN- γ 上升→抑制TH2分泌IL-4,IL-13活化b cell及IgE的分化→過敏反應降低

(A)選項不是我的範圍看審稿組有沒有要更改的)

(B)符合第二項→易患過敏反應

(C)較早接觸病原菌的小孩較不易有過敏, 因TH1活化會抑制TH2, 可參考共筆衛生假設的部分→過敏反應降低

(D)住在農村裡, 應與第一項西方化社會相反→過敏反應降低

所以如果改成Which of the following "is" the risk factor for asthma? 答案就是(B)

8. Delayed type hypersensitivity的發生需要多久時間? 【M103】

(A)30min內 (B)1~2小時 (C)24~72小時(D)24~30天

Ans: (C) 共筆p.27 CH14 PPT37圖

1.Which of the following is the most effective cytokine for proliferation and differentiation of eosinophils? 【M102/CM103】

(A)IL-4 (B)IL-5 (C)IL-12 (D)IFN-r

解: B, PPT24的表格中, IL-3、IL-5、GM-CSF都有此功能

(D) 3. Hyper-IgM syndrome type I results from the defect of ____.

A. CD40 expression on B cells

B. CD40 expression on T cells CD40(B) <=> CD40L(T)

C. CD40L expression on B cells

D. CD40L expression on T cells [見共筆第四頁第八點]

(D) 4. Which of the following mechanisms is the major cause of Ab affinity maturation?

A. Antigenic competition

B. DNA recombination

C. Large amount of Ag administration

D. Somatic hypermutation[見考古題名詞解釋第四題0.0]

(B) 5. Which of the following molecules is NOT one of the B-cell co-receptor molecules?

A. CD19

B. CD20

C. CD21

D. CD81 [CD19, CD21, CD81為B-cell coreceptors; CD20 is Ca²⁺ channel]

(C) 6. The most commonly transplanted organ is ____.

A. bone marrow

B. liver

C. kidney

D. skin

(C) 7. Which of the following molecules is the C3 convertase of the complement classical pathway?

A. C3b

B. C3bBb

C. C4b2a

D. C4b2a3b

(D) 13. A secondary immune response is more rapid and intense than a primary response.

The most likely explanation of this observation is that:

A. antigen persists longer in the secondary response.

B. antigen presentation is more rapid in the secondary response.

C. a pool of cells which specific class I MHC proteins is generated during the primary response.

D. a pool of both memory B cells and memory T cells is generated during the primary response.

6. Which of the following approach can NOT be considered as the potential treatment for asthma?

(A) blockade of IgE receptor (B) inhibit IL-12 (C) lipoxygenase inhibitors

(D) the use of CpG oligodeoxynucleotides IL-12 induce Th1 production

8. Which of the following description is NOT correct for type III hypersensitivity?

(A) Ab-Ag immune complex initiates the reaction.

(B) ADCC is the major reaction for tissue destruction.

(C) The reaction causes serum sickness.

(D) Ab-Ag complex can be cleared in liver.

3. Compare to the protective immunity, which of the following is the typical character of oral tolerance?

(A) induced by toxins

(B) specific serum Ab can be detected

(C) could induce the activation of Th3 cells

(D) with memory responses

6. What is the best reason for the lack of Ab specific to Kb molecule in the F1 mice of anti-Kb transgenic mice cross to liver-specific Kb-expressing mice?

(A) deletion of anti-Kb B cells in bone marrow

(B) induction of T regulatory cells

(C) the anergy of anti-Kb B cells in peripheral tissues

(D) deletion of anti-Kb B cells in peripheral tissues

7. You have isolated a protein from a plant that some of your patients might be allergic to its leaves. Which of the following character would confirm that this protein is an allergen?

(A) with protease activity

(B) high solubility

(C) positive on skin test

(D) small molecular weight

7. How long does it take to develop type IV granulomatous hypersensitivity?

(A) 30 minutes (B) 6-12 hours (C) 48-72 hours (D) 21-28 days

9. Which of the following is NOT the risk factor for asthma?

(A) be the first child in a family

(B) be infected with intracellular bacteria

(C) has a SNP (single nucleotide polymorphism) linked to IRF (interferon regulatory

factor) gene

(D) live in an industrialized society

三.名詞解釋：

1. linked-recognition 【M104】 【CM104】 (課本p808)

T_H cell可以活化B cell的一種規則。B cell和 T_H cell必須辨認來自相同antigen上的epitopes(可以是不同epitopes,但必須是結構上相連的一個整體抗原)。

3.FcRn

一種receptor可以把帶IgG通過胎盤，結構與MHC1相似，兩個FcRn對一個IgG，也可以維持血漿中的IgG level

1.intraepithelium lymphocyte 【CM105&M104】

淋巴細胞位於epithelium層的黏膜表面則稱之，主要為T細胞，且IEL在腸道多為CD8 T cell，可以殺死被感染的細胞

2.M cell 【M104】

在小腸epithelium層，有一種特化的表皮細胞，主要功能為將抗原送到表皮下方，使B cell 和T cell產生免疫反應
補充：表面無絨毛和glycocalx，且本身不會分泌任何的消化酵素

3.hygiene hypothesis 【M104】

清潔理論假說，從小生長在過於乾淨的環境，會使免疫系統中的輔助型T cell趨向分化為 T_H2 ，使得增加日後發生過敏的機率。

4.wheal-and-flare response 【CM105】

過敏反應時因histamine會作用，導致立即性的血管通透性增加，造成水腫或導致局部表面血管擴張，即皮膚變紅。以上所造成的皮膚損傷稱為wheal-and-flare response (可參考課本第588頁)

6.Celiac disease(1%) 【M103,CM105】

屬於第四種過敏反應，由麵粉中的gluten所引起，造成消化道上皮慢性發炎，摧毀小腸絨毛，降低消化道的吸收能力，病人時常拉肚子。

1.Immunoprecipitation 【M104】 (不再範圍內吧!)

免疫沉澱法：以蛋白質為抗原，並以可以與此蛋白質專一性結合的抗體，從含有多種蛋白質的樣品中，分離並且濃縮出自己想要的蛋白質。

2.Autoinflammatory disease 【M103】

自體免疫疾病，未受感染卻有發炎反應，可能有很多原因，如遺傳基因缺陷等等。

3.Secondary lymphoid follicle 【M103】

次級淋巴濾泡，為lymph node中有germinal center形成的部分。B細胞在此進行somatic hypermutation和class switch，最後達到affinity maturation。

1. Thymus-independent antigen

Thymus-independent (TI) antigens可以直接刺激B cell產生antibody不需Th cell。TI又分為type 1和type 2。

Type1 antigen多為microbial origin(cell wall component) (eg., LPS)。活化後的B cell沒有affinity maturation, 沒有記憶性、不會class switch (只產生IgM)、不會somatic hypermutation，此外TI-1 Ag量多的時候可行polyclonal activation，一次活化多種B cell。

Type 2 TI antigen則多為polymeric protein antigens，與type 1不同在於若有cytokine刺激，可以產生IgG，但是不能行polyclonal activation。且TI-1可以刺激mature & immature B cell, TI-2大多只能刺激mature B cell。

2. B-cell co-receptor

為一組在B cell上穿膜的signaling receptor，由CD19、TAPA-1和CD21(CR2)組成。在co-receptor的幫助下，B cell receptor的效率可增強上百倍。可降低訊號傳遞閾值、減少活化B cell所需的抗原數。CD19有ITAM, CR2是complement receptor

3. Inhibitory B-cell co-receptor

有些B cell的membrane molecules containing immunoreceptor tyrosine-based inhibition motifs (ITIMs) in the cytoplasmic region (eg., FcγRIIB), ITIM會recruit & activate phosphatase (eg., SHP-1, SHP-2) 以抑制B cell receptor signaling。ex.CD22

4. Ab affinity maturation

B cell在分裂的過程中，因為有hypermutation的特性，製作出對其specific Ag有不同親和力的子代，經過selecion後，使得Ab對Ag的結合能力越來越好，這現象稱之為affinity maturation

5. Centroblast

被活化的B cell會往 primary lymphoid follicle跑，並形成germinal center中的dark zone，centroblast其實就是B cell開始要活化的狀態，是一群能快速分裂的B細胞，每6-8小時可複製一次，large size, expanded cytoplasm, diffuse chromatin, 沒有surface Ig。centroblast會分化成尺寸較小、有表面Ig且不再分裂的centrocytes，被FDC吸引到light

zone。

6. Subcapsular sinus macrophage

顧名思義是駐守在subcapsular sinus的macrophage,吞嚥力差,分解力也差,可以把Ag保留在膜上並轉給FDC。

(1)將Ag保留在其膜上，讓B cell encounter

(2)保留Ag，使之能被送進follicle並localized 在follicular dendritic cell上

7. Toxoid

modified toxins, lack of toxic activity but retain receptor-binding site。

8. Passive immunization

取自實驗動物，將具有抗某種疾病的免疫血清注射到人體內，使病人迅速獲得對該病的抵抗力，注入人體的為antibody而非antigen。免疫力產生快，免疫時效短；重覆使用則可能產生過敏性反應。Antibody存在時間短，在人體內過一段時間後，就會逐漸被分解而消失。

1. Airway remodeling

呼吸道的肌肉層和黏膜層因為長時間的發炎反應而增厚的現象，最後痊癒會發展成纖維化

5. Rheumatoid factor

是一種anti-IgG autoantibody。只要可以辨認自身“IgG之Fc片段”的IgM, IgG和IgA等抗體即屬之，簡單來說，就是可以辨識自身抗體的抗體。

4. hypo-sensitization (specific allergen immunotherapy)

是指將高劑量的過敏原注入皮下，幫助病人產生對過敏原的tolerance並幫助病人的B cell 去製造IgG抗體而不是IgE

6. oral tolerance 口腔黏膜對一般的食物具有耐受性，不會引起免疫反應，但是對疾病抗原就會引起免疫反應。

the capacity of the immune system to recognize substances taken in through the digestive system and to weaken or suppress the immune response to them

7. Farmer's lung

a hypersensitivity pneumonitis，因吸入了來自稻草等農作物的粉塵孢子，與在體內的IgG形成複合物堆積在肺泡內影響肺功能。屬於type III hypersensitivity

8. serum sickness

(serum sickness)也是一種典型的第三型過敏反應，其Ag為一種serum protein，進入血液後與體內的抗體形成免疫複合體，導致發燒、血管炎、關節炎、腎炎等等，而這些現象都是暫時性的，一旦免疫複合體被清除後，就會消失。

9. rhogam

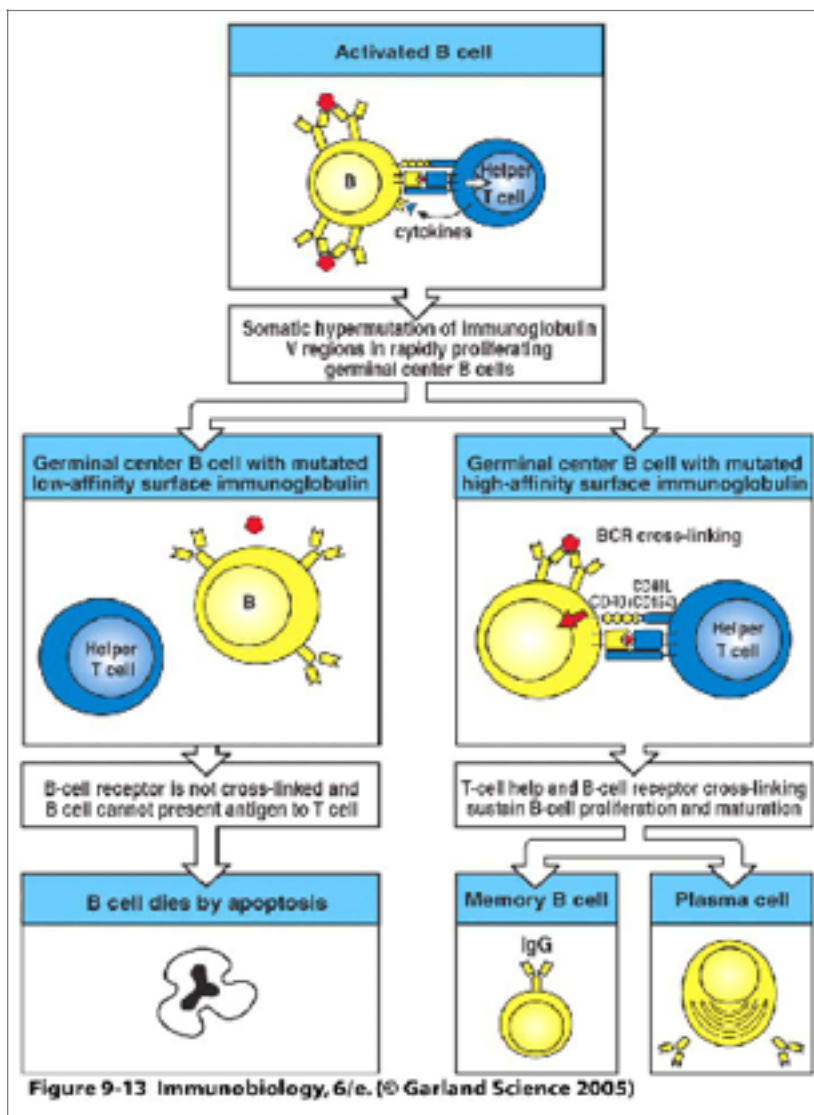
要對Rh陰性的母親施打，他會與胎兒Rh Ag結合，防止媽媽的B cell看到此Ag，這樣便不會產生memory cell跟Ab啦。因此再生第二胎的時候就不會有抗體出來攻擊胎兒的紅血球了。

10. delayed-type hypersensitivity

直接注入皮下的抗原經APC吞嚥呈現後，活化Th1上的MHC class II，使Th1分泌許多cytokine召喚其他免疫細胞及引起血管擴張造成該處的發炎反應。

四. 簡答題

1.解釋affinity maturation過程與機制,place?



1. B cell 在follicle border被結合抗原的T cell 活化後而遷移到germinal center。
2. Somatic hypermutation導致胺基酸在Ig V regions發生取代作用而影響到B cell的命運。

左圖：

3. 導致B-cell receptor對抗原親和性變低，使B cell無法有效率被活化，因B-cell receptor cross-linking與 B cell將胜肽抗原呈現給T cell的能力均會下降。
→此導致B cell apoptosis
→大部分的變異不是陰性就是中性，因此在 germinal center會有大量B cell死亡及增生

右圖：

3. 有些變異會改善B-cell receptor結合抗原的能力，此可增加B cell與T cell發生反應的機會，因此增殖並存留下來。
→存活下來的細胞會經歷不斷突變及選擇而分化成memory B cell or plasma cell，並離開 germinal center

2. Compare and contrast mature resting B cells, plasmablasts and plasma cells in terms of their proliferation, surface Ig and MHC class II, antibody secretion, and class switch? 【M102/CM103】

Ans:

| | Property | | | | | |
|---|------------|----------------------|------------------------|-----------|-----------------------|----------------|
| | Intrinsic | | | Inducible | | |
| B-lineage cell | Surface Ig | Surface MHC class II | High-rate Ig secretion | Growth | Somatic hypermutation | Isotype switch |
| Resting B cell | High | Yes | No | Yes | Yes | Yes |
| Plasmablast | High | Yes 也還有B7 | Yes | Yes | Unknown | Yes |
| Plasma cell (condensed chromatin, prominent rough ER, Golgi apparatus) | Low | No | Yes | No | No | No |

Figure 9-10 Immunobiology, 6/e. (© Garland Science 2005)

1. Resting B cell: 表面顯現出專一性免疫球蛋白(通常是IgM、IgD)及MHC class II 分子，V區基因無somatic mutation。這些受體可攝取抗原並將之呈現給helper T cell，誘使B cell增殖、isotype switch、somatic hypermutation，但在此期間B cell不會分泌抗體。

2. Plasmablast: 屬中間表現型，可分泌抗體，但仍具表面免疫球蛋白及MHC class II 分子，因此可持續攝取並呈現抗原給helper T cell。
3. Plasma cell: 可產生抗體的B cell，不再與helper T cell發生反應，因缺膜型免疫球蛋白及MHC class II 分子，亦無法isotype switch或發生更進一步的somatic hypermutation。

3.請舉出3個antibody對抗infection的作用

Neutralization：抗體結合毒素並且中和之，使其不能跟身體的細胞結合造成傷害

Opsonization：抗體包住抗原，使抗原容易被辨認，增加吞噬能力

Complement activation：活化補體，可增強吞噬，也可直接破壞細菌

1.List two characteristics of intraepithelial lymphocyte(2%)【M103】

- A. 位在epithelial層
- B. 具有 $\alpha\epsilon$ ： $\beta 7$ integrin
- C. 大部分為CD8 T cell，可分為兩類，分別是CD8 $\alpha\beta$ 和CD8 $\alpha\alpha$

2.Describe how epithelial cells play a critical role in innate defense against pathogens. (5%)【CM105&M103】

| | Skin | Gut | Lungs | Eyes/nose |
|------|----------------------------------|------------|----------|----------------------|
| 機械性 | Epithelial cell以tight junction連接 | | | |
| | 空氣和液體的縱向流動 | | 纖毛造成黏液移動 | 眼淚/鼻腔的纖毛 |
| 化學性 | 脂肪酸 | 低ph值 | | 眼淚中的酵素 (lysozyme) |
| | | 酵素(pepsin) | | |
| | 抗菌肽 | | | |
| 微生物性 | 正常菌落 | | | |

(此題老師上課沒教，共筆可是看起來是這個範圍的= =，答案為參考CM104/M103)

3.Describe 2 routes of IgA antibody gain access into intestinal lumen.【M102&CM103】

A.IgA與小腸表皮細胞底部的poly-Ig receptor結合，經由epithelial cell 被transcytosis到腸腔內

B.Hepatobiliary route：血液中的IgA經過hepatic portal vein時，被分泌到bile caniculus，混入膽汁內(此次上課沒教，答案為參考CM104/M103)

4.我們是否可利用Treg cell在周邊達到clonal anergy的效果？為什麼？(大意)

因為Treg的產生壓抑了免疫反應(TGF- β 也可以調控B cell促使IgA的產生,並阻止class switch)

CH12 PPT21 (這啥不再範圍內吧= =)

5.Describe "Hygiene hypothesis" for the development of allergic diseases?(4分)【CM103】

我們的免疫系統有兩類的輔助型T cell， T_H1 和 T_H2 ，這兩類細胞一般在免疫系統內達成平衡，不過T細胞在分化的過程中，來自細菌或病毒的感染會強化趨向 T_H1 的反應，相對的減弱 T_H2 的反應，而 T_H2 是偏向過敏反應。簡而言之，這個假設是說在T細胞分化的嬰幼兒時期，過於清潔的環境，減少了對免疫系統 T_H1 的刺激，使免疫系統偏向 T_H2 分化，也就強化了日後的過敏反應發生的機率。

7.In addition to anti-inflammatory mediators and 減敏療法, describe 3 potential methods and the mechanisms for the treatment of asthma.【M103,可參考CH14 PPT25,28】

- A. Anti-IgE: omalizumab→ block IgE receptor
- B. IL-12, CpG等促使 T_H1 路徑抑制 T_H2
- C. 透過抑制IL-5來block cytokine和chemokine受體，避免eosinophil的活化。

3. Delayed-type hypersensitivity的sensitization phase 和 effector phase.【CM105】老師好像沒有教

Ans: <小編:遲發性過敏反應中的effector phase應該就是指elicitation phase>

A.Sensitization—第一次遇到抗原時，抗原呈現細胞(APC)將之呈現給淋巴結中的T細胞，活化T細胞並產生memory T cells.

B.Elicitation—再次遇到抗原時，抗原呈現給memory T cells，T細胞釋放cytokines.

1. Please contrast and compare the characteristics of IgA and IgG (4%)【CM105】

| | IgA | IgG |
|--|-----|-----|
|--|-----|-----|

| | | |
|------------|---|--|
| Properties | 1. 主要存在於mucosa(體內最多)，亦存在於母乳裡 2. transport across epithelium 3. 形成dimer | 1. 體液中都有，是serum內最多的Ig 2. transport across placenta ，供胎兒前6個月保護 3. 為monomer |
| functions | 皆可進行neutralization、opsonization及活化補體系統 | |

2.epithelium cell 在Innate immunity的重要性【CM105】

[第12次共筆，PPT16]

epithelium cell 上具有TLR及NOD的受器，它接受到刺激後活化NFκB。

轉錄因子NFκB使epithelium cell表現大量免疫相關的化學分子(chemokines, cytokines)，活化中性球、MΦ跟DC。

TLR=Toll-like receptor

TLR-4 :認LPS

TLR-5 :認flagella

NOD= Nucleotide-binding Oligomerization Domain(屬Nod-like receptor)

NOD1 認 gram (-)

NOD2 認 gram(+)&gram(-)

3.細胞凋亡與自體免疫疾病的關係(3%)【CM105】

解：

- 當antigen被消滅掉之後，effector cell就會因為Fas和FasL的結合而進入 apoptosis，只要留下memory cell就好。假如effector cell數量沒有下降的話(例如FasL基因出問題)，很可能就會引起自體免疫疾病。
下面兩個是沒有明文表示但我認為應該也會有關的：
- 當細胞老化或凋亡時，細胞膜會內縮形成apoptotic body，讓macrophage去吞噬，是身體裡正常的代謝功能。→胞內的self-antigen一直包在膜裡，不會暴露出來，self ag也就不會活化lymphocyte而引起自體免疫疾病
- 在免疫豁免區中，會有FasL的表現，若有誤入此區的淋巴球，FasL與淋巴球上的Fas相接就會使淋巴球apoptosis。若此機制被破壞，則有可能引發自體免疫疾病。

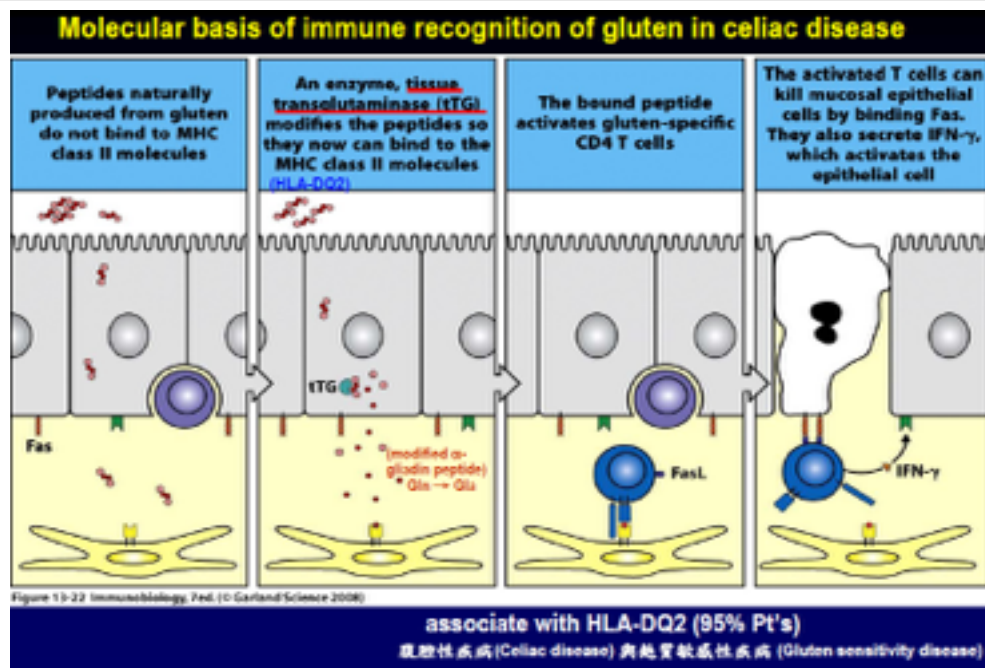
不過如果她只給三分的話我覺得寫(1)應該就可以了。

4.Compare and contrast the properties and functions between IgM and IgG(6%)【M103】

| | IgM | IgG |
|------------|---|---|
| Properties | 1. 最快產生出來的Ig，代表急性感染期，存在時間較短 2. 主要存在於淋巴液和血液 3. transport across epithelium 4. 形成pentamer | 1. 需較久時間才能產生出來，代表過去或最近曾有的感染，存在時間長(可終生) 2. 體液中都有，是serum內最多的Ig 3. transport across placenta ，供胎兒前6個月保護 4. 需經過class switch才能產生 |
| functions | 同為活化補體重要的抗體 | |
| | 在急性期活化補體，活化補體能力最強 | 主導neutralization、opsonization，促使NK cell進行細胞毒殺 |

5.請描述Celiac disease牽涉的molecular mechanism?【M102/CM103】

屬於第四型過敏反應，由專一性T_H1和CD8 cytotoxic T細胞所主導。由抗原進入身體的方式可分成三種症候的其一：Gluten-sensitive enteropathy (**celiac disease**)。



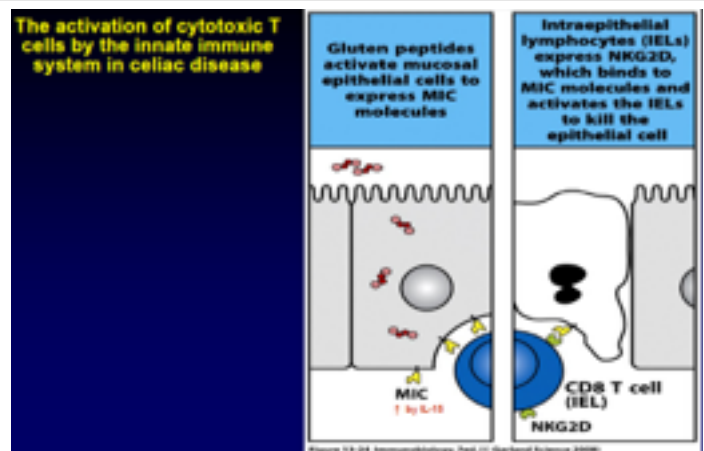
Gluten-sensitive enteropathy (celiac disease)

有些人吃麵粉類的東西會拉肚子，因為麵粉內含gluten。

- Gluten中的主要成分α-gliadin被tTG酵素(tissue transglutaminase) modify，改變了上面的胺基酸，方能接上MHC class II (HLA-DQ2)，活化專一性T cell。T cell會用Fas ligand和上皮細胞的Fas結合，殺死黏膜上皮細胞，還會釋放cytokines引起腸道發炎。

- 另外celiac disease也可以被innate immune system的胞殺性T細胞啟動反應：

Gluten peptides會刺激黏膜上皮細胞表現MIC分子(MHC class Ib molecules)，與CD8Tcell (=IELs=intraepithelial lymphocytes)所表現的NKG2D結合，MIC就會活化IELs殺死腸道上皮細胞。腸胃道受損就容易拉肚子了。



- **Compare thymus-dependent (TD) antigen with thymus-independent (TI) antigen**
 需靠T細胞才可活化B細胞 VS 不須靠T細胞
 屬soluble protein VS 細菌細胞壁的成分或polymeric protein
 可引起isotype swithing、affinity maturation、memory VS 都不可

1. **Describe how commensal bacterial can prevent inflammatory responses in the intestine.** (3%) 一般來說病原會被TLR辨識，活化IKK，IKK磷酸化IκB，使其被降解，釋放NFκB進入細胞核促進轉錄。可是共生菌會活化PPARγ，將NFκB從細胞核中移除，防止轉錄。或者是阻止IκB被分解，讓NFκB沒辦法進入細胞核

1. Describe how the immune complex is removed from circulation.

Ab: Ag complex在血液中形成並活化complement，導致大量C3b與其結合。將RBC上的CR1 receptor會與C3b結合，將complex帶到spleen或liver，而spleen和liver中的phagocyte藉由FcR與complex結合活化，將complex移除。

2. Please list the three types of purified macromolecules that are currently used as vaccines.

Capsular polysaccharide, toxoid, & recombinant surface antigen.

3. type III hypersensitivities are characterized by immune complex deposition. Describe the clinical consequences of immune complex deposition.

第三型過敏反應主要由免疫複合體(Ag-Ab complex)的堆積所引發的局部發炎反應(Local inflammatory response)，又稱 **Arthus reaction**。其mechanism主要由在組織中的free Ag與free Ab結合形成免疫複合體，結合後便會刺激該處mast cell上的FcγRIII使mast cell degranulation，釋放出細胞內發炎物質，導致該處產生發炎反應，有名的疾病像是Farmer's Lung即是一例。

4. Describe the difference between the early and the late response in asthma

Early:發炎物質促使黏液分泌和平滑肌收縮，導致呼吸道阻塞，最大呼氣流量會急劇下降

Late: cytokines and eosinophil products造成血管擴張，有edema的現象，最大呼氣流量比正常低，但慢慢恢復正常

3. In the germinal center reaction, centroblasts and centrocytes cycle between the light and dark zone. regulate this movement and activity factors? (2%)

Centroblast at dark zone

Centrocyte at light zone

Dark zone中有stromal cell會分泌CXCL12，吸引有CXCR4的centroblast進駐，執行proliferation、mutation變成centrocyte後，會受CXCL13的吸引(因為有CXCR5)進入light zone進行selection、class switching、differentiation。而少部分的centrocyte仍保有CXCR4的表現，因此會再回到dark zone繼續循環。

4. Discuss how dendritic cells in the intestine are distinct from their counterparts in other tissues, and describe how their functions are adapted to the local challenges faced by the immune system in the gut.

對於共生菌和致病菌有不同調節方法

在有共生菌、TGF等存在時會抑制DC的成熟，不成熟的DC只能給出weak co-stimulatory signal，induce CD4 T cell differentiate into Treg

當致病菌穿越上皮活化DC，DC就會表現strong co-stimulatory signal, induce CD4T differentiate into Th1 and Th2