SIRS and SEPSIS

臨床數據判讀與護理意涵課程

邱艷芬教授

Review of Human defense

人体免疫系統

先天性免疫: 第一道防線
後天性免疫: 自感染恢復後才引發

humoral immunity

soluble factors:

- complement
- antibodies

cell mediated immunity

cells:

•PMN
•monocyte
•lymphocyte

先天性免疫

先天性免疫(innate immunity)
免疫力不因重覆感染而增強, non-specificity

Soluble factor
- lysozyme
- complement
- acute phase proteins
  eg. CRP, interferon

Cells
phagocytes:
- PMN
- monocytes
- natural killer cells

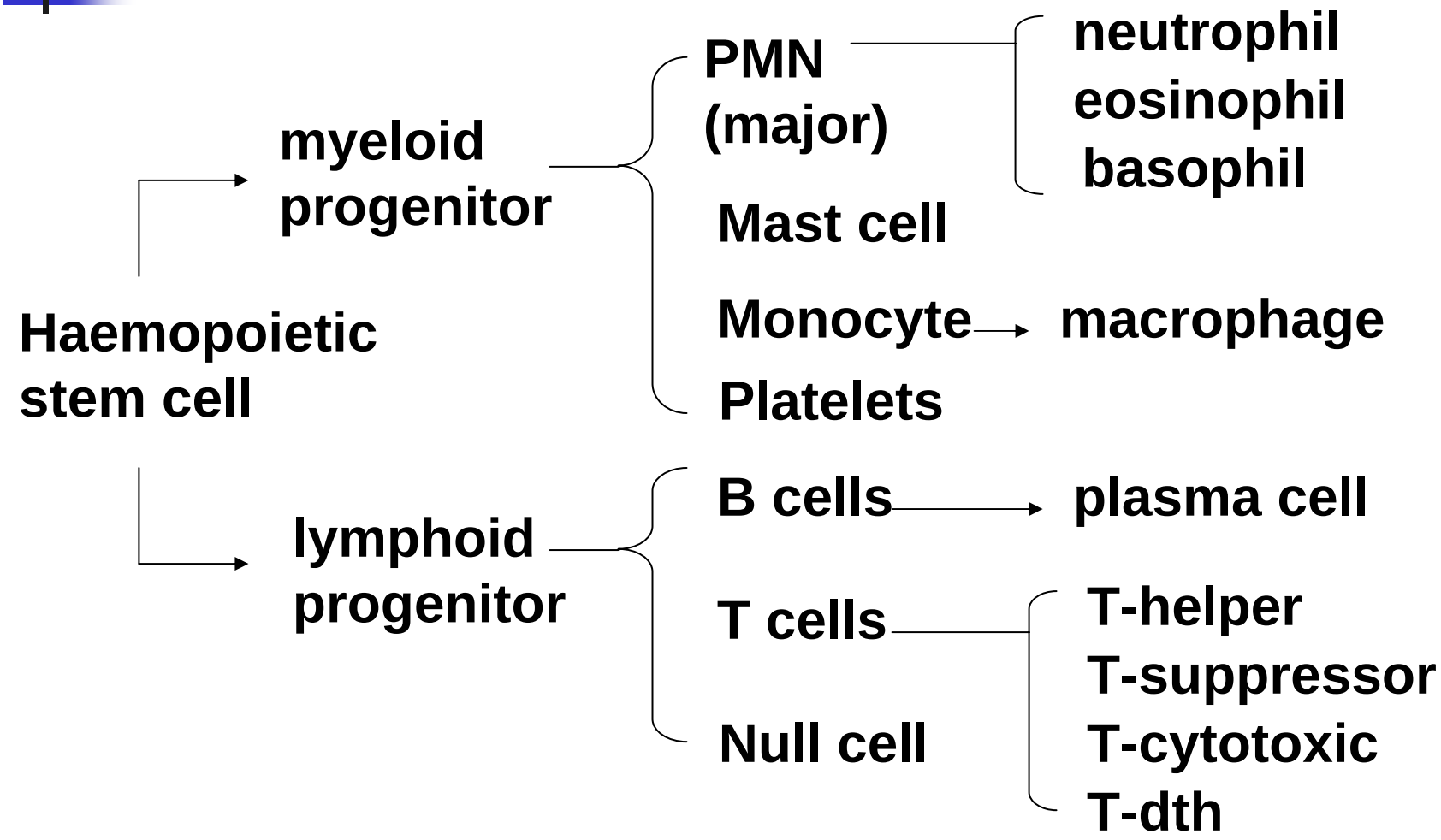
後天性免疫

後天性免疫(adaptive immunity)
免疫力會因重覆感染而增強, specificity

Soluble factor
- antibodies

Cells
T lymphocyte cell
B lymphocyte cell

免疫細胞的製造


Haemopoietic stem cell
myeloid progenitor
PMN (major)
neutrophil
eosinophil
basophil
Mast cell
Monocyte
macrophage
Platelets
lymphoid progenitor
B cells
plasma cell
T cells
T-helper
T-suppressor
T-cytotoxic
T-dth
Null cell

各 Soluble factors之功能

⇨補體(complement):結合在細菌上,藉下列功能促進吞噬細胞之功能:

1)溶解細胞膜

2)吸引吞噬細胞 (chemotaxis)

3) opsonization (蛋白質包裹促進吞噬作用之過程)

⇨C-reactive protein:

覆在微生物上促進補體連接

⇨干擾素(interferon):

1) 激活natural killer cells,加強其殺滅功能

2) 誘發未感染組織對病毒的抵抗性

PMN

⇨ polymorphonuclear neutrophils

- neutrophil: 殺滅吞入之有機體
- basophil and mast cell:

在allergen 刺激下, 釋出heparin, SRS-A 與 Eosinophil 趨化因子-A

- eosinophil:

殺滅吞入之有機體，釋出histaminase 與 acryl sulfatase, 以鈍化mast cell減少其製造histamin 與 slow reactive substance of anaphylaxis (SRS-A), 抑制發炎反應。

Monocytes

⇨ macrophage 前身

- Reticuloendothelial system, RES

  Resident macrophage,

  skin, lymph node, kidney, spleen

  lung, liver, brain

- Circulating blood monocytes (macrophage)

Lymphocyte

⇨ 20~25%% of WBC

- T cell:

  helper-T, cytotoxic-T, suppressor-T

- B cell: 5-15% of 循環淋巴球，促使 plasma cell，製造antibody

表面存在內生性抗體

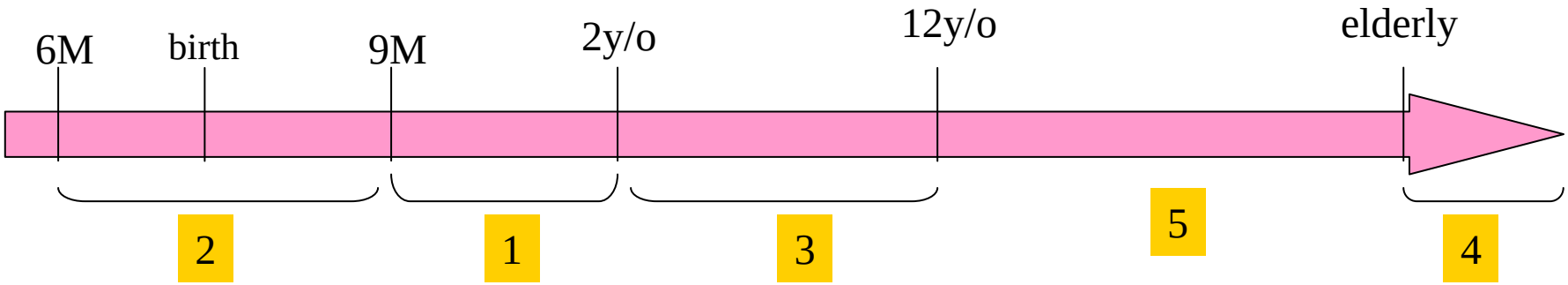
- IgM: 5~10%,
  早期反應, 為primary response之主要抗體
  在B cells表面，輸血反應之主要immunoglobin
- IgD: 0.2%, 在B cells表面
- IgG: 最多, 佔免疫球蛋白70%-75%,
  為secondary response之主要抗體,
- IgA: 5~15%, in mucus secretion
- IgE: 0.5%, 在basophil and mast cells 表面, 與過敏有關

人體內生性抗體之製造

- IgG可得自母體，母體之IgG於九個月時消失
- 胎兒自六個月大起可自行製造IgM，出生後又可自行製造IgG, IgA，
- 達成年人濃度：

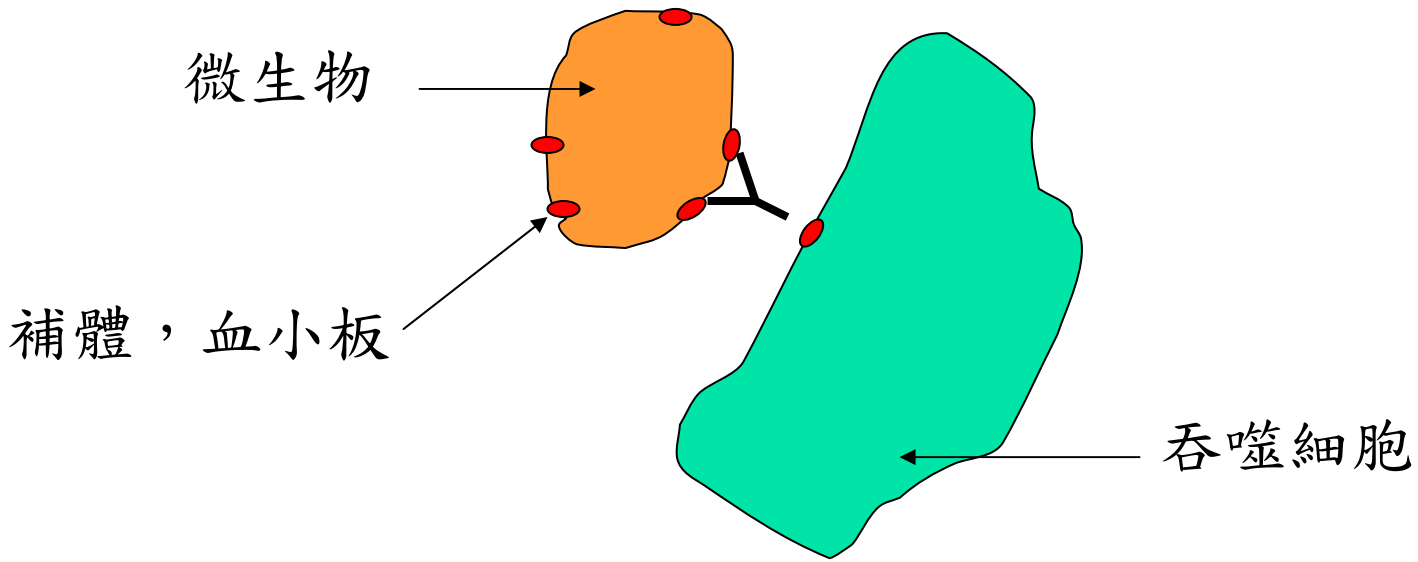
  IgG最快，約於2歲時，

  IgA最慢，約12歲時



Antibody:

與微生物結合 (antigen binding portion - Fab),
攜至吞噬細胞 (bind by Fc portion)



Null cells and Platelets

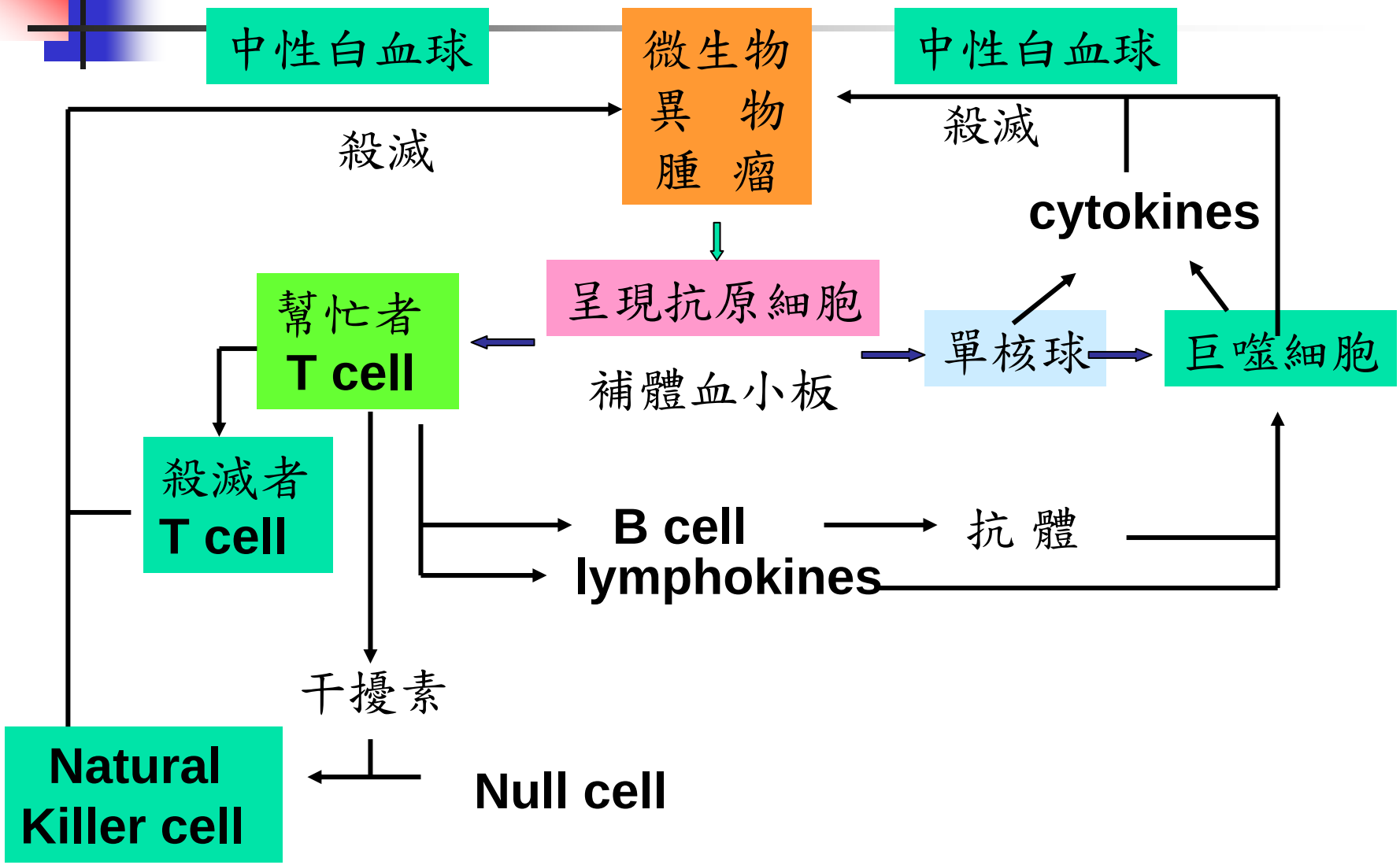
⇨non-T, non-B cell, natural killer cells (NK)

⇨platelets :

表面有IgG 與 IgE之受體(receptor)

可釋出permeability-increasing substance並活化補體以吸引白血球

免疫功能之運作


中性白血球
微生物
異　物
腫　瘤
中性白血球
殺滅
殺滅
cytokines
呈現抗原細胞
幫忙者
T cell
單核球
巨噬細胞
補體血小板
殺滅者
T cell
B cell
抗 體
lymphokines
干擾素
Natural
Killer cell
Null cell

Life-threatening infection

Sepsis

Bacteremia: 血中有死或活的細菌

Endotoxemia: 血中有內毒素

Septicemia: 血中有細菌與內毒素

Septic shock

感染

經由循環

自一組織傳至另一組織，引起

全身炎症反應

與

循環衰竭現象

人體對抗感染之防禦系統

三道防線

第1道: 網狀內皮系統

第2道: 中性白血球

第3道: 巨噬細胞

網狀內皮系統

- tissue macrophage: 存在於各組織的網狀細胞(reticular cells)將入侵之微生物先trap住，加以殺滅。
  - 肝: Kupffer cell
  - 腸: gut associated lymphoid tissue (GALT)
  - 腦: microglia
  - 肺泡: alveolar macrophage
  - 淋巴球、脾、骨髓、皮下組織

- 屬first line of defense
  營養不良時，這些reticular cells的質與量均減

中性白血球

- 循環血液中之neutrophil藉chemotaxis快速至感染處，將微生物胞圍吞噬:

  polymorphoneuclear neutrophil (PMN) activation(promoted by opsonin which may used off in critically ill)

- 屬second line of defense
- 此時也將引起neutrophil增生，造成血中白血球增生現象

巨噬細胞

- 由單核球來，噬菌力強，為neutrophil16倍
- 屬third line of defense
- 此時需更多之monocyte轉成macrophage，造成血中單核球增生現象

Factors impede host defense

1. 植入物與異物
   increase irritation to tissue
   increase risk for inflammation and infection

2. 用藥
   antibiotics change microflora
   glucocorticoids抑制發炎反應、引起淋巴細胞分解、減少抗體合成

Factors impede host defense

3. 組織灌流不良

   組織對抗細菌之能力減弱, 增加感染可能

4. 長期營養不良

   免疫細胞萎縮，生產量減少，活動力差，吞噬力弱

5. 腸道廢用

   腸粘膜萎縮屏障力弱，易引起Bacterial Translocation

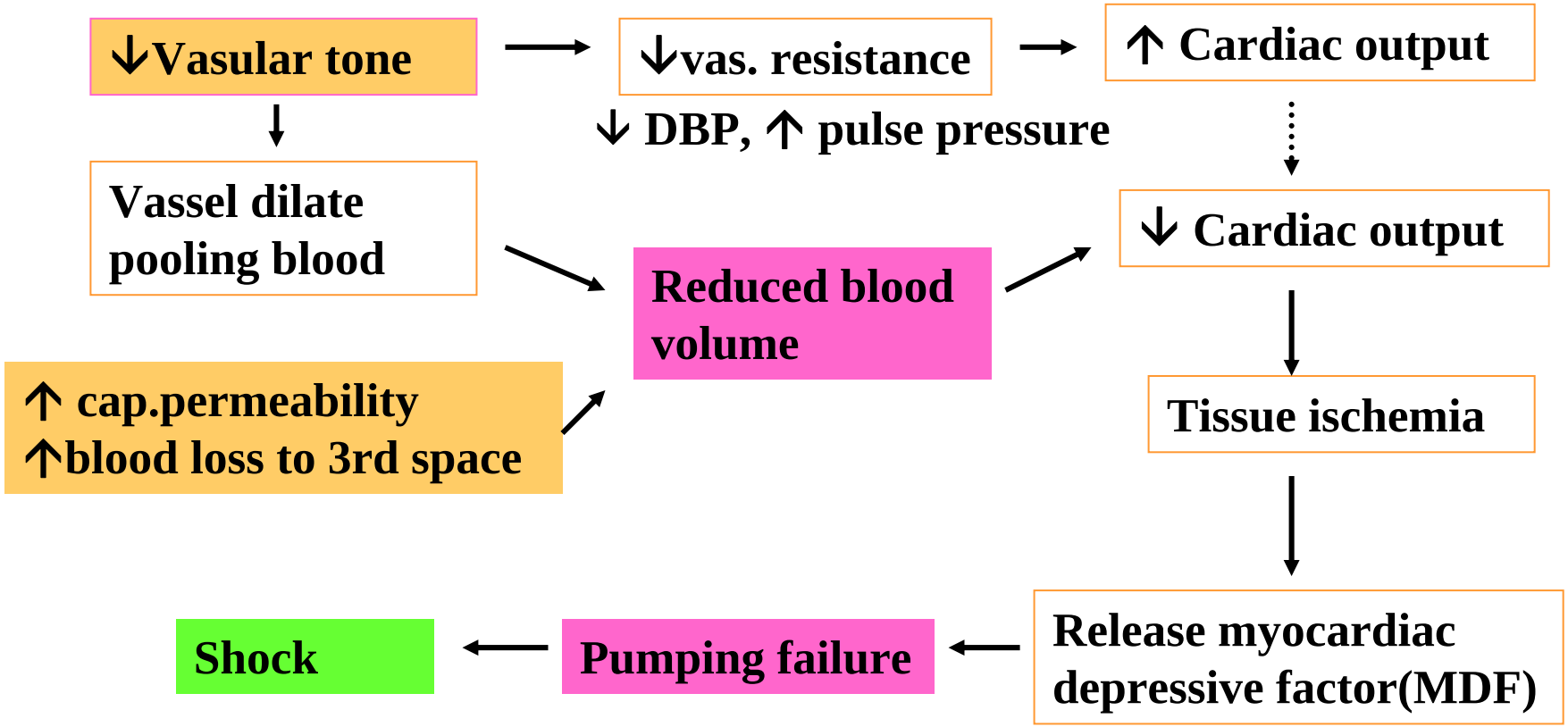
炎症反應

- vasodilation:

  increase circulation to invaded area
- increase capillary permeability
- chemotaxis: attract WBC to invaded area

- 局部炎症反應造成該部位充血，引起紅、腫、熱、痛
- 當全身均發生炎症反應時, 水份滲出可引起嚴重之血循改變

From sepsis to septic shock



Pathophysiological response of sepsis

- inflammation
- Endotoxin response
- Host response
- hemodynamic response

發炎反應

組織釋放vasodilator peptide: histamin, serotonin, acetylcholine, bradykinine, catecholamine，造成

- vasodilate: bring PMN and antibodies to eliminate invading organism
- increase capillary permeability
- lysis cellular component
- chemotaxis: attraction of neutrophils

Endotoxin response

- inactivate or block RES

  ⇨鈍化第一道防線

- 影響受sympathetic nerve支配的血管,

  ⇨ vassel spasm, pooling of blood, anoxia

  ⇨decrease vascular tone

Host response

Endocrine response

⇨ increase ADH:

water retention, decrease U/O (oligurea)

⇨ decrease insuline function, increase glucagon, catecholamine,

⇨ increase aldosteron: by renin-angiotension system: increase Na, decrease K

Host response

- Asidobase
  - Metabolic acidosis: 因缺氧
  - Respiratory alkalosis: 因hyperventilation
  - Hyperventilation的原因：endotoxin對呼吸中樞的影響，代償 metabolic acidosis
- Organ
  - Lung: 細胞性缺氧，降低compliance, 增加呼吸功與分流
  - CV: 減少循環血量，增加動靜脈壓力，增加心室壓力
  - Kidney: 減少 GFR
  - GI: 增加水份流失到腸腔、引起ileus

Hemodymanic response

Hyperdynamic	Normadynamic	Hypodynamic
warm, dry, pink	peripheral edema	**cold clammy skin**
flushed skin	increased RR	
decreased PaO2	decreased PaO2	
tachycardia	tachycardia	tachycardia
CO↑	normal CO,	**CO↓**
PVR ↓, DBP ↓	PVR ↓	PVR ↑
CVP ↓	CVP ↓	CVP ↓
pulse p >40	25-30	20
increase lactate	Resp.alkalosis	**meta. Acidosis**
U/O ↓ ↑	U/O ↓	
	microthrombi, DIC	

Assessment of septic shock

Three physiological indeces:

1. decrease SBP 80-90 mmHg
2. U/O $<$ 25 ml/hr
3. metabolic acidosis

Warning signs

1. ↓DBP, ↑ pulse pressure
2. ↓ urine output
3. R. alkalosis→M. acidosis

Management

1. Fluid treatment

Lactated Ringer

rapid 500 cc in 20 minute, then 200 cc in 15 min, until S/S of overload

Keep PCWP ＜12㎜Hg, CVP＜ 10㎝H2O

2. Medications

necessary when

1). SBP＜70㎜Hg for 30 min after fluid replaced

2) Lung/kidney poor organ perfusion

3) poor cardiac output

SIRS

- Systemic Inflammatory Response Syndrome
  - An inflammatory process exceeding level of paracrine activation damages vascular endothelium & parenchymal cell
  - Hyperdynamic, hypercatabolic
- **Criteria (Bone, JAMA 1992; 268: 3452-5)**

  Two or more of the following clinical signs of systemic response to endothelial inflammation:
  - BT>38℃ or <36℃
  - HR>90/min
  - RR>20/min or $PaCO_2$<32mmHg
  - WBC>12000/mm^3 or <4000/mm^3 or band form >10%

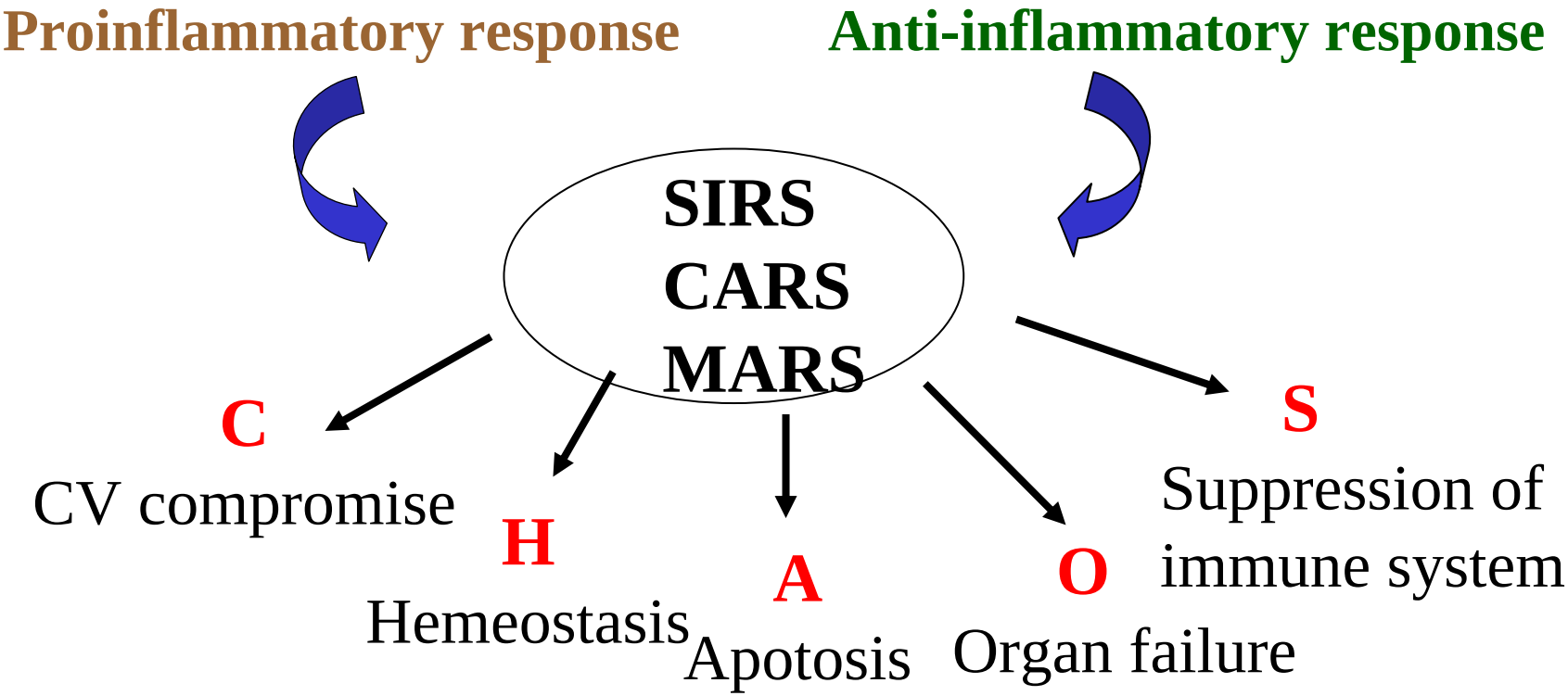
名詞定義

SIRS	有兩個或兩個以上所定義的臨床徵狀
Sepsis	**SIRS 加上証實有感染者**
Severe sepsis	**SIRS 加上証實有感染者，並累及血液動力之失去穩定**
MODS	器官功能無法維持生理平衡的一種混亂性生理狀態

SIRS to MODS

Proposed Mechanism

- Varying stage of a malignant intravascular inflammatory process



**CARS：compensatory anti-inflammatory response syndrome

MARS：mixed antagonist response syndrome

SIRS vs. Infection

- Confusing !
  - 感染的徵象如體溫增高WBC增加在trauma但無感染之病患也有
  - SIRS 的全身性徵象在感染與未感染個案間並無不同
- Dilemma !
  - 對感染者未加治療可導致器官衰竭與死亡
  - 對所有SIRS病人都投予抗生素，使未感染病患不必要的接觸抗生素，倘若未來發生嚴重G(-) 院內感染時，治療將更不容易

研究案例討論

Miller PR. ,Munn DD. , Meredith JW., Chang MC.

Systemic inflammatory response syndrome in **the trauma intensive care unit**:

who is **infected**?.

Journal of Trauma-Injury Infection & Critical Care. 47(6):1004-8, 1999.

Purpose of the article

- to examine the ability of CRP to identify infectious versus noninfectious causes of SIRS
- To compare the descriminate ability of CRP with WBC and maximum temperature (Tmax) in this respect.

Immune Index and data management

- CRP, Tmax, and WBC值
  - 在感染組取被診斷為感染之首日
  - 非感染組(在ICU期間無感染)取住ICU之第五天 (感染組被診斷為感染之平均天)
- 以receiver operating characteristic (ROC) curves檢視各參數之區辨力
- 在全部個案及SIRS個案均進行檢視分析SIRS.

Discriminating power

	Entire group		SIRS group	
Infection	Sens	Spe	Sen	Spe
CRP >17	74%	75%	72%	100%
T_{max} >102º F	67%	80%	72%	83%
Both			91%	50%

CRP normal 0–1.0 mg/dl