
بسم الله الرحمن الرحيم
اللهم إِيَّاكَ نَعْبُدُ وَ إِيَّاكَ نَسْتَعِينُ

ایمونولوژی دستگاه تنفس

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lungs : structure and function

Lungs evolved as efficient gas-exchanging apparatus

UPPER AIRWAYS Conducting airways (2cm2 cross-section)
- up to 23 bifurcations, trachea, bronchi, bronchioles

LOWER AIRWAYS Gas exchange (75m2 cross-section)
- respiratory bronchioles, 300 million alveoli

Large mucosal surface
- 9000 L of air per 24hr at rest
- filtration of entire cardiac output.

Lungs are fairly sterile suggesting very efficient protection.

Table 1 List of lung diseases from the American Lung Association and their relations to host defense

Name of the lung disease	Definition of disease	Relation to host defense
Acute bronchitis	Inflammation of the bronchial tubes	Usually direct
Asbestosis	Scarring of lung tissue as a result of breathing in asbestos fibers	Pathway involved
Asthma	A lung disease that makes it harder to move air in and out	Pathway involved
Bronchiolitis	An inflammation of the bronchioles	Pathway involved
Bronchopulmonary dysplasia	A lung disease that occurs most often in premature babies	Indirect
Byssinosis	A lung disease caused by exposure to dusts from cotton processing, hemp, and flax	Pathway involved
Chronic bronchitis	Chronic inflammation of the airways or bronchial tubes	Pathway involved
Coccidioidomycosis	An infection of the lungs caused by inhaling spores of the fungus *Coccidioides immitis*	Direct
Chronic obstructive pulmonary disease	Also known as emphysema and chronic bronchitis	Pathway involved
Cryptogenic organizing pneumonia	A disease in which the bronchioles and alveoli become inflamed with connective tissue	Pathway involved
Cystic fibrosis	An inherited disease that causes thick, sticky mucus in the lungs, pancreas, and other organs	Pathway involved
Emphysema	A lung disease that makes it hard to breathe	Pathway involved
Hantavirus pulmonary syndrome	A disease that comes from contact with infected rodents or their urine, droppings, or saliva	Direct
Histoplasmosis	An infection in the lungs caused by inhaling the spores of the fungus *Histoplasma capsulatum*	Direct
Human metapneumovirus	Infections that cause colds, pneumonia or bronchitis	Direct
Hypersensitivity pneumonitis	A disease in which lungs become inflamed when a patient breathes in certain fungal dusts	Pathway involved
Influenza	A serious respiratory illness caused by infection with three influenza virus families: A, B, or C	Direct
Lung cancer	The second most commonly diagnosed cancer and the most common cause of cancer death	Pathway involved
Lymphangiomatosis	A disease of the lymphatic system	Indirect
Mesothelioma	An uncommon form of cancer that involves the mesothelium	None
Nontuberculous mycobacterium	An infection caused by mycobacteria that are found in water and soil and only infect some people	Direct
Pertussis	A respiratory infection caused by the bacteria *Bordetella pertussis*	Direct
Pneumoconiosis	An occupational lung disease caused by inhaling coal dust	Indirect
Pneumonia	A common lung infection caused by bacteria, a virus, or fungi	Direct
Primary ciliary dyskinesia	Blockage and infections caused when mucus accumulates due to cilia dysfunction	Direct
Pulmonary fibrosis	A disease marked by scarring in the lungs	Direct
Pulmonary vascular disease	A disease that affects the blood circulation in the lungs	None
Respiratory syncytial virus	The most common cause of bronchiolitis and pneumonia in children younger than age one in the United States	Direct
Sarcoidosis	A disease caused by small areas of inflammation	Direct
Severe acute respiratory syndrome	A disease caused by a group of viruses called the coronaviruses	Direct
Silicosis	A disease caused by inhaling tiny bits of silica	Direct
Tuberculosis	A common infectious disease caused by various mycobacteria, usually *Mycobacterium tuberculosis*	Direct

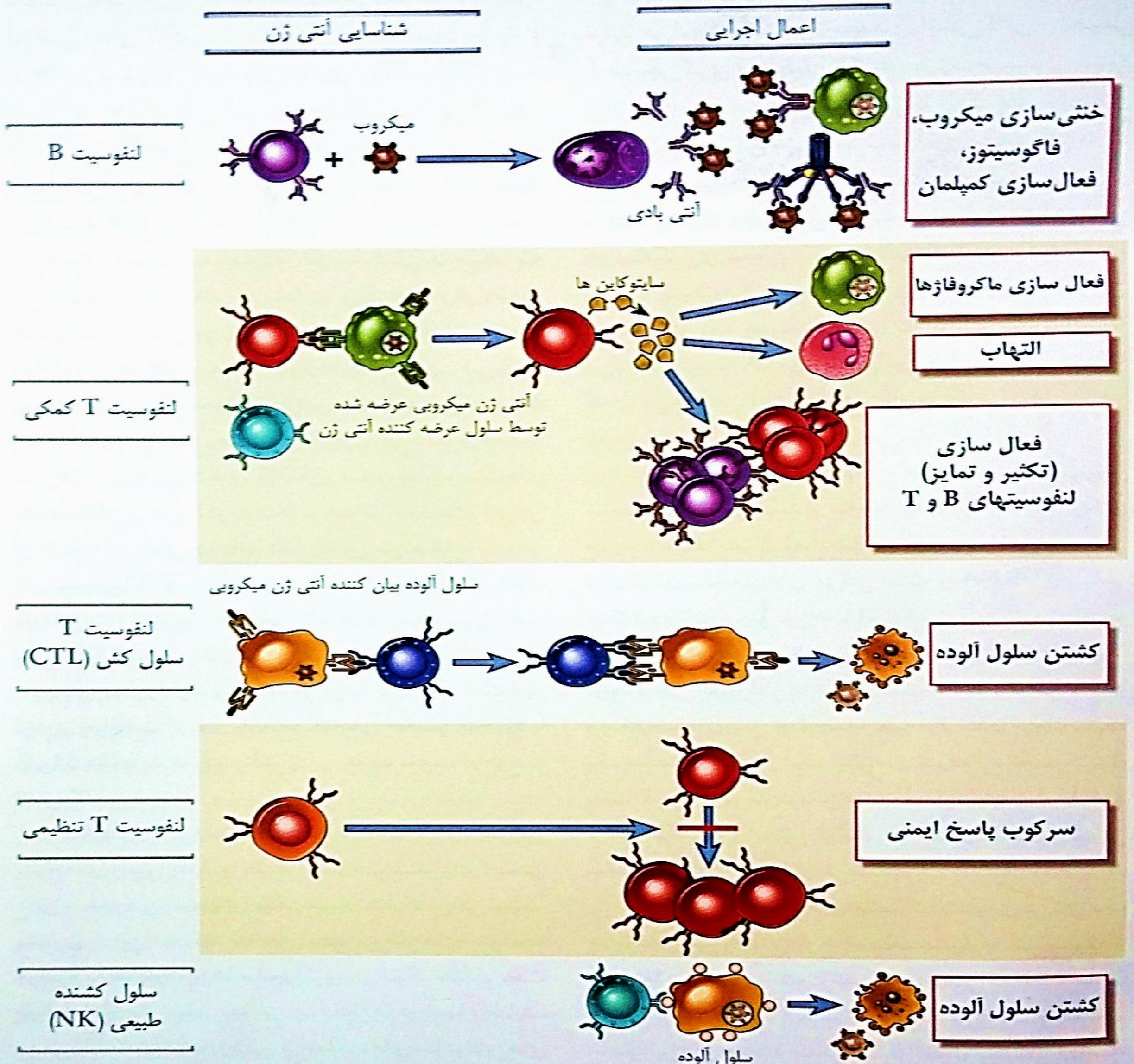
why study lung immunology

Global burden of disease

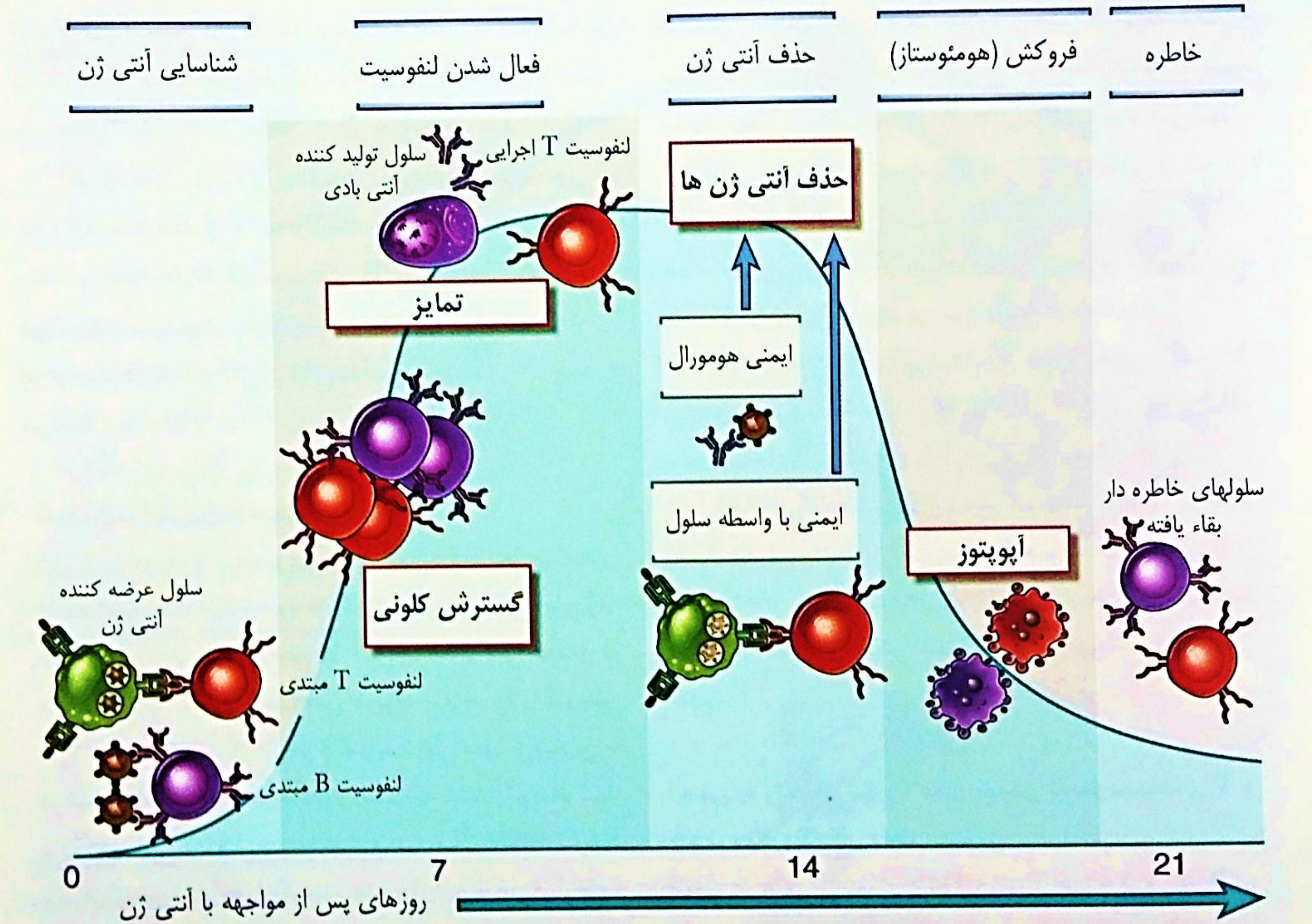
Rank		% total
1.	pneumonia	8.15
5.	COPD*	2.77
7.	tuberculosis	2.1
30.	asthma	0.78

*chronic obstructive pulmonary disease

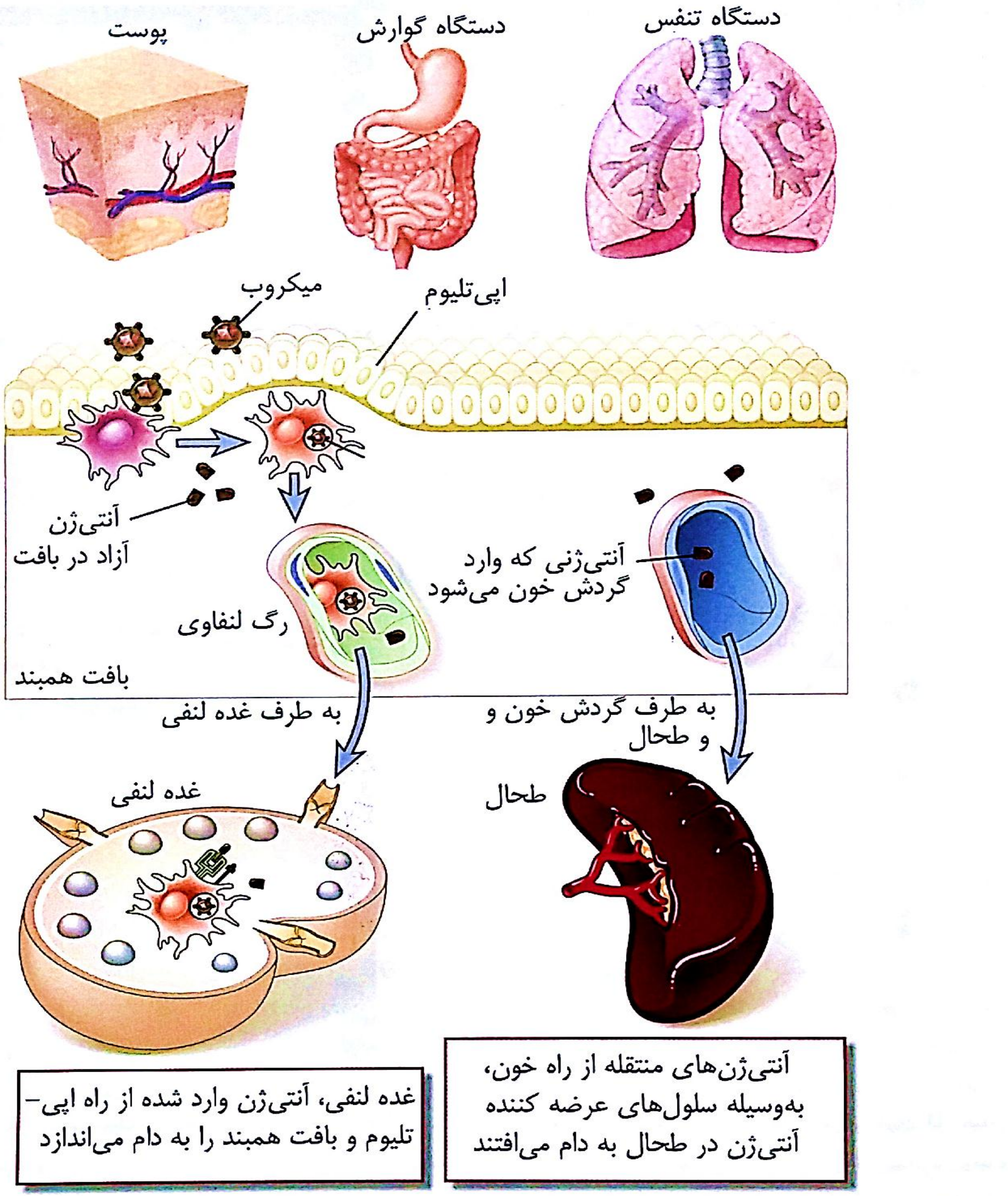
Ashley RV. 2000 Economic Perspectives on Vaccine Needs



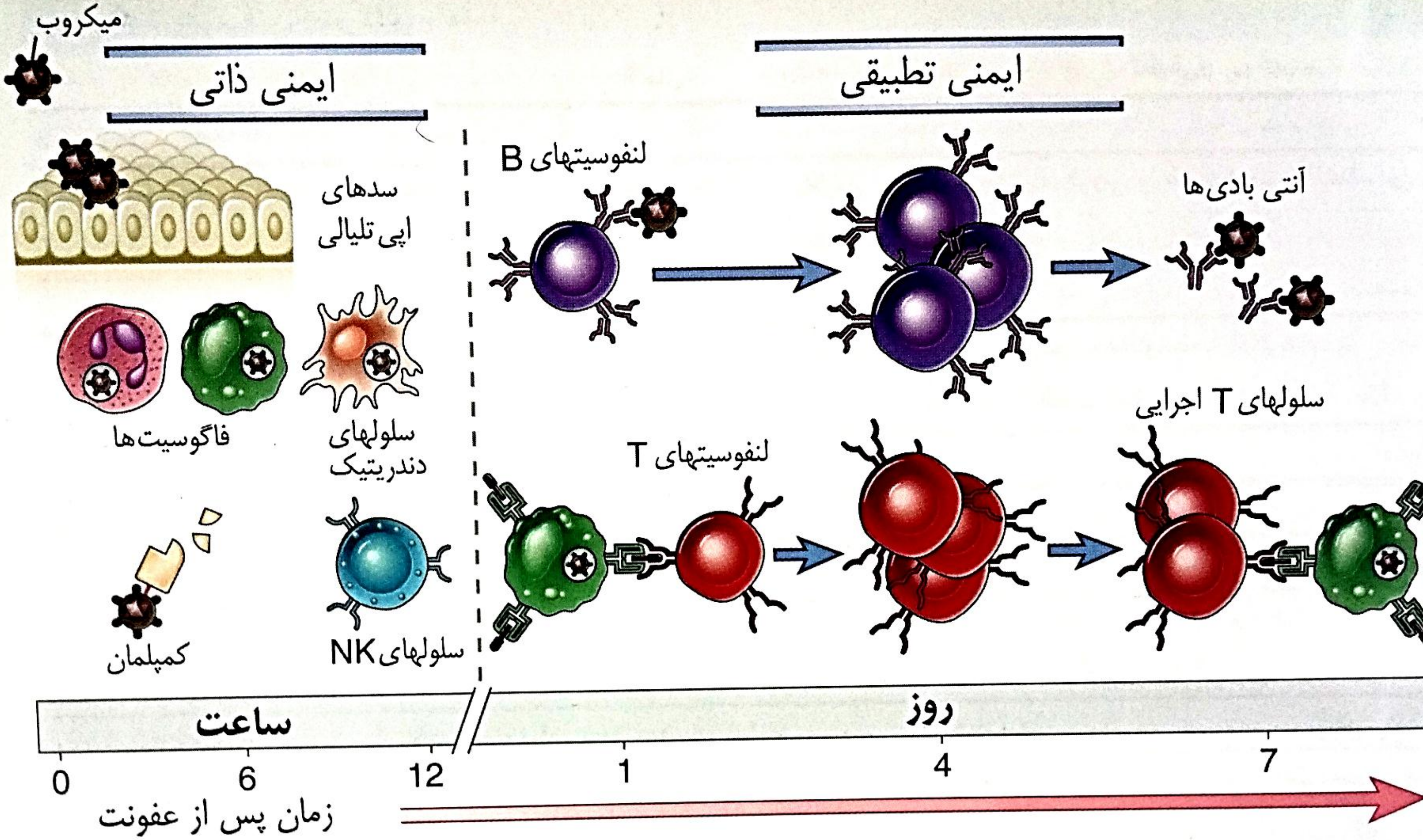
شکل ۵-۱ دستجات لنفوسیتی. لنفوسیت‌های B با شناسایی آنتی‌ژن‌های محلول به سلول‌های ترشح‌کننده آنتی‌بادی تبدیل می‌شوند. لنفوسیت‌های T کمکی با شناسایی آنتی‌ژن‌ها بر سطح APCها به ترشح سایتوکاین‌ها می‌پردازند که مکانیسم‌های مختلف ایمنی و التهاب را تحریک می‌کنند. CTLها با شناسایی آنتی‌ژن‌های سطح سلول‌های آلوده موجب تخریب این سلول‌ها می‌شوند. سلول‌های T تنظیمی پاسخ‌های ایمنی بر علیه آنتی‌ژن‌های خودی را سرکوب نموده و از ایجاد آن ممانعت به عمل می‌آورند. سلول‌های NK حاوی گیرنده‌های آنتی‌ژنی با تنوع محدودتری نسبت به گیرنده‌های آنتی‌ژنی سلول B و T هستند که با شناسایی اهداف خود (مثلاً بر سطح سلول‌های آلوده) به کشتن این سلول‌ها مبادرت می‌ورزند.



شکل ۶-۱ مراحل پاسخ‌های ایمنی تطبیقی. پاسخ‌های ایمنی تطبیقی از مراحل مختلف تشکیل شده‌اند که سه مرحله اول آن عبارتند از: شناسایی آنتی‌ژن، فعال‌شدن لنفوسیت‌ها و حذف آنتی‌ژن (مرحله اجرایی). پاسخ‌ها با آپوپتوز لنفوسیت‌های تحریک‌شده با آنتی‌ژن فروکش می‌کنند (مرحله افول) که منجر به هومئوستاز شده و آن تعداد از سلول‌های اختصاصی آنتی‌ژن که باقی می‌مانند، مسئول ایجاد خاطره می‌باشند. مدت زمان هر مرحله در پاسخ‌های ایمنی مختلف، متفاوت است. محور عمودی، معیاری قراردادی برای بیان شدت پاسخ است. این اصول برای ایمنی هومورال (با واسطه لنفوسیت‌های B) و ایمنی سلولی (با واسطه لنفوسیت‌های T) صادق می‌باشد.



شکل ۳-۶ مسیرهای ورود آنتی‌ژن. آنتی‌ژن‌های میکروبی عموماً از طریق پوست، دستگاه گوارش و دستگاه تنفسی وارد بدن شده و در مبادی ورودی توسط سلول‌های دندریتیک به دام افتاده و به گره‌های لنفاوی ناحیه‌ای منتقل می‌شوند. آنتی‌ژن‌هایی که وارد گردش خون می‌شوند توسط APCهای موجود در طحال به دام می‌افتند.



شکل ۱-۱ ایمنی ذاتی و تطبیقی. مکانیسم‌های ایمنی ذاتی، دفاع مقدماتی را بر علیه عفونت‌ها ایجاد می‌کنند. پاسخ‌های ایمنی تطبیقی پس از آن ایجاد شده و با فعال شدن لنفوسیت‌ها همراه می‌باشند. زمان‌بندی پاسخ‌های ایمنی ذاتی و تطبیقی، به صورت تخمینی نشان داده شده و در عفونت‌های مختلف، متفاوت می‌باشد.

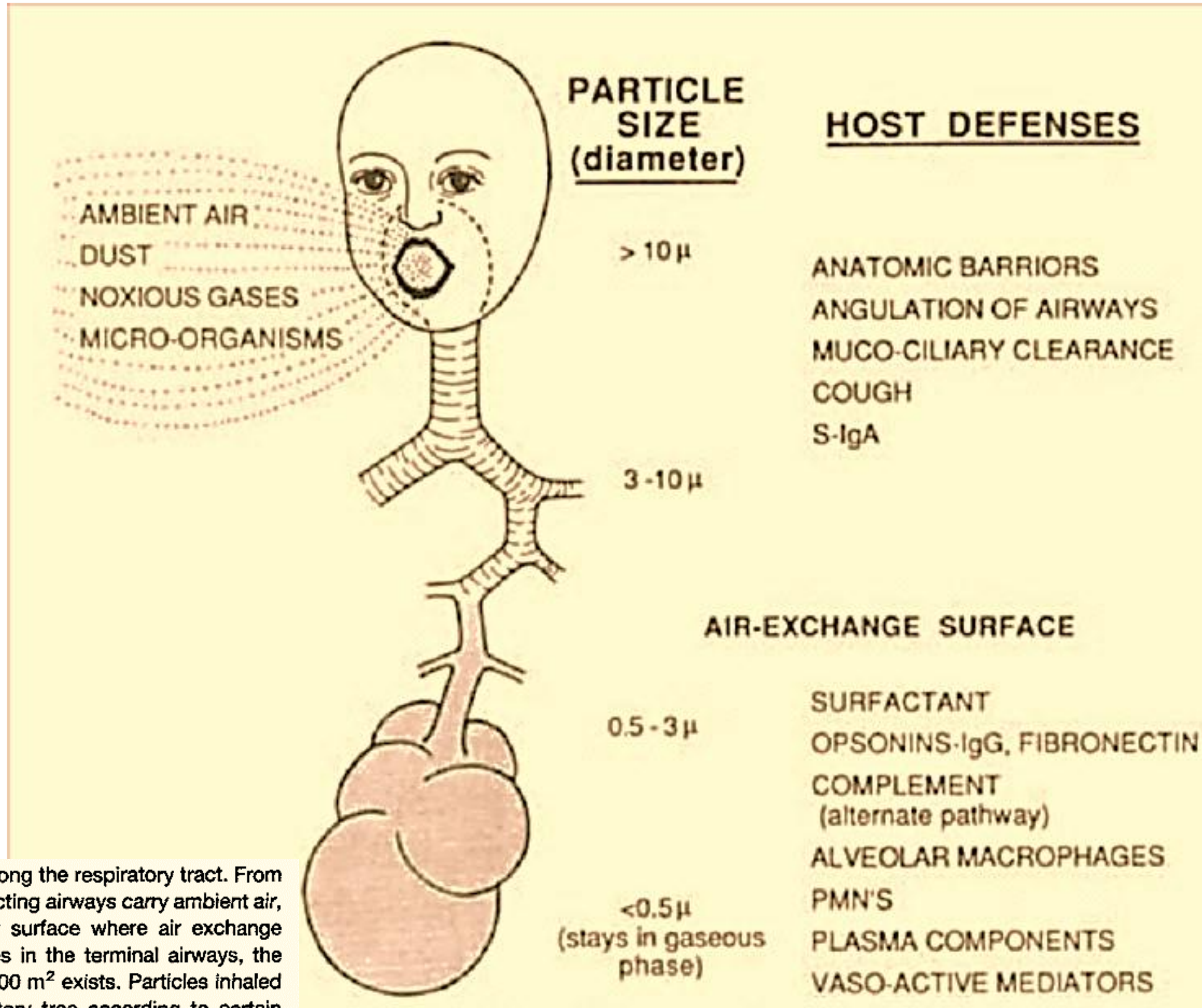


Fig. 1. Spacial relationship of host defenses along the respiratory tract. From the site of air intake at the nose and mouth, conducting airways carry ambient air, airborne particles, and microbes to the alveolar surface where air exchange occurs. Below the level of respiratory bronchioles in the terminal airways, the alveolar space, representing a surface area of ~100 m^2 exists. Particles inhaled with air either segregate at levels in the respiratory tree according to certain aerodynamic dimensions or impact against the mucosa at branching points of the trachea and bronchi. Microbes, especially the bacteria, are of a size (<3 μm diameter) that can reach the alveolar surface. Host defenses in the upper airways principally consist of mechanical barriers (such as the larynx or air stream turbulence at branching points) and the mucociliary clearance mechanism. Beyond the level of the respiratory bronchioles, however, phagocytes and other soluble factors (opsonins) are needed to cleanse the alveolar surface. (From Reynolds[1] with permission.)

Alcohol Clin Exp Res, Vol 19, No 1, 1995: pp 6–10

دلایل حضور پراهمیت عوامل دفاعی در تشکیلات تنفسی

برخورد دائم با مواد و آنتی ژنهای بیولوزیک و شیمیایی

کل خون در گردش، از ریه عبور نموده و پالایش می شود---تماس سلولهای ایمنی با آنتی ژنها و پارتیکل های موجود در گردش هوای تنفسی

وجود گردش لنفاوی دائم و حضور بافت های لنفاوی پریفرال (لوزه ها ......)

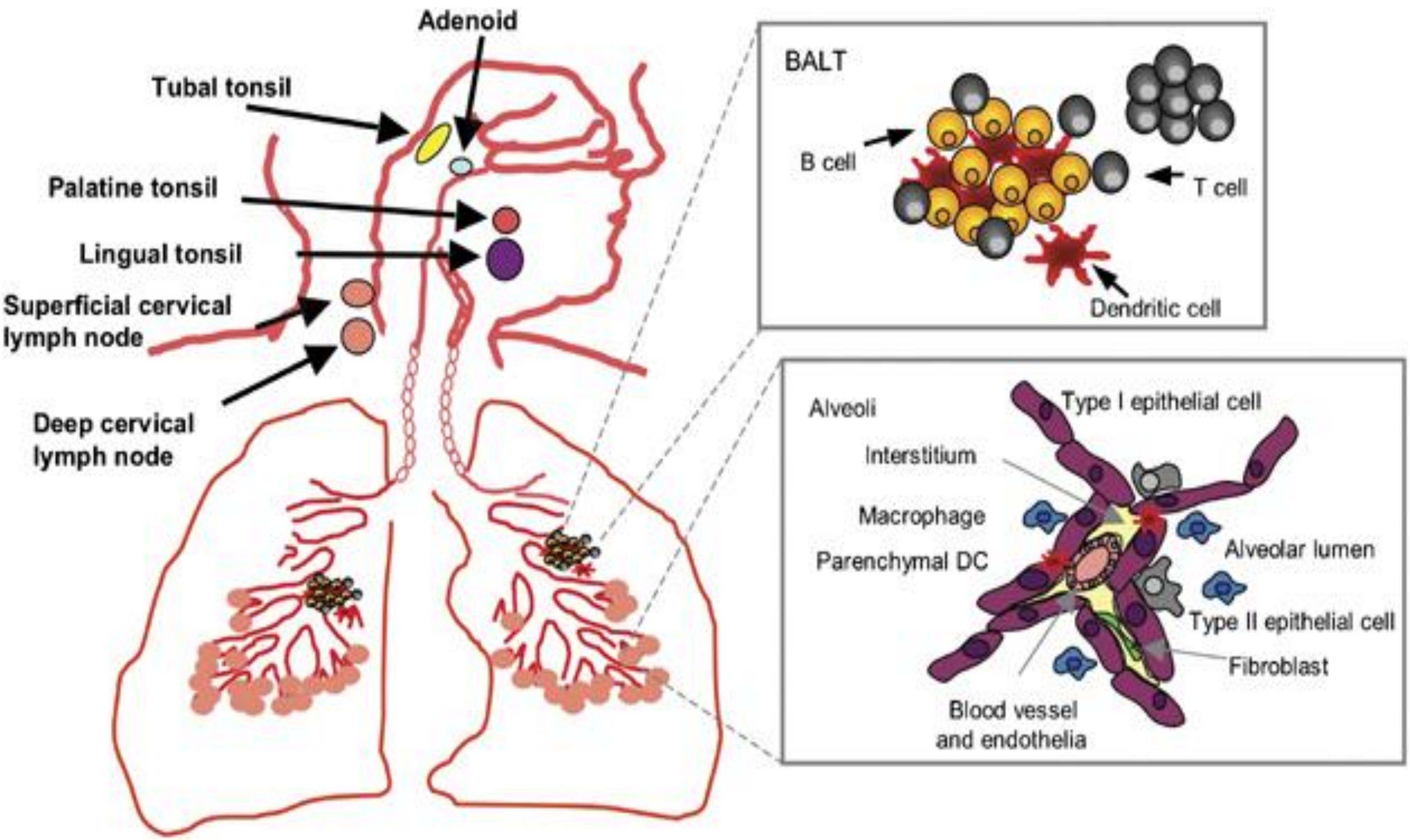
لزوم استقرار دائم و ایمونوفیزیولوژیک ایمنی موضعی (در فضای آلوئولار ، در بافت بینابینی، در سراسر لولة تنفسی)

ظهور پاسخ های ایمونولوژیک در دستگاه تنفس = بروز التهاب، عفونت و یا پاسخ ایمنی گردند.

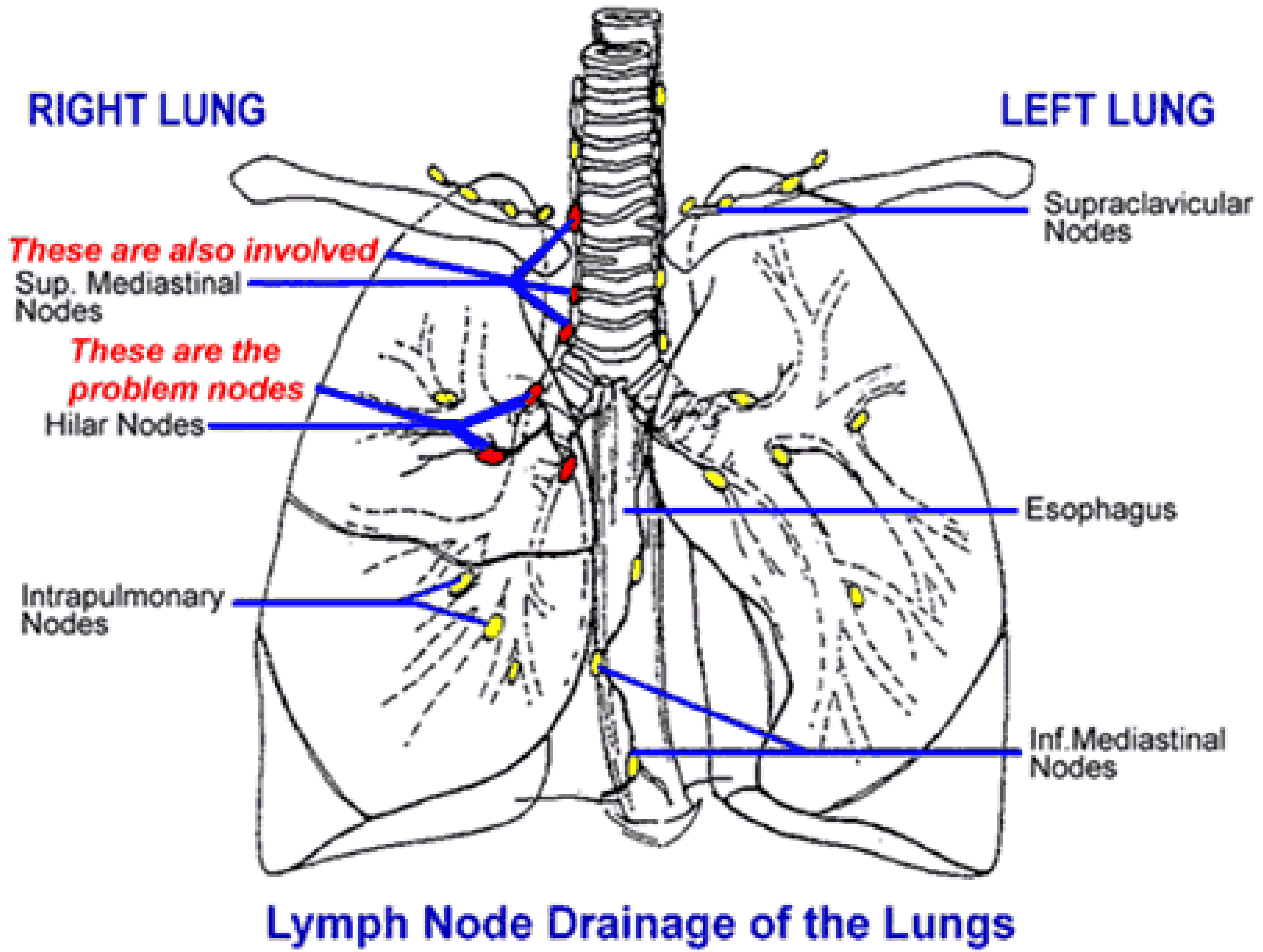
بافت ریه می تواند مورد آسیب و ضایعات ایمونوپاتولوژیک بسیاری قرار گیرد

مطالعة مایعات حاصل از لاواژ برونکوآلوئولر(تجربی ، بالینی تشخیصی)

اعضای لنفاوی مرتبط



Lung lymph nodes



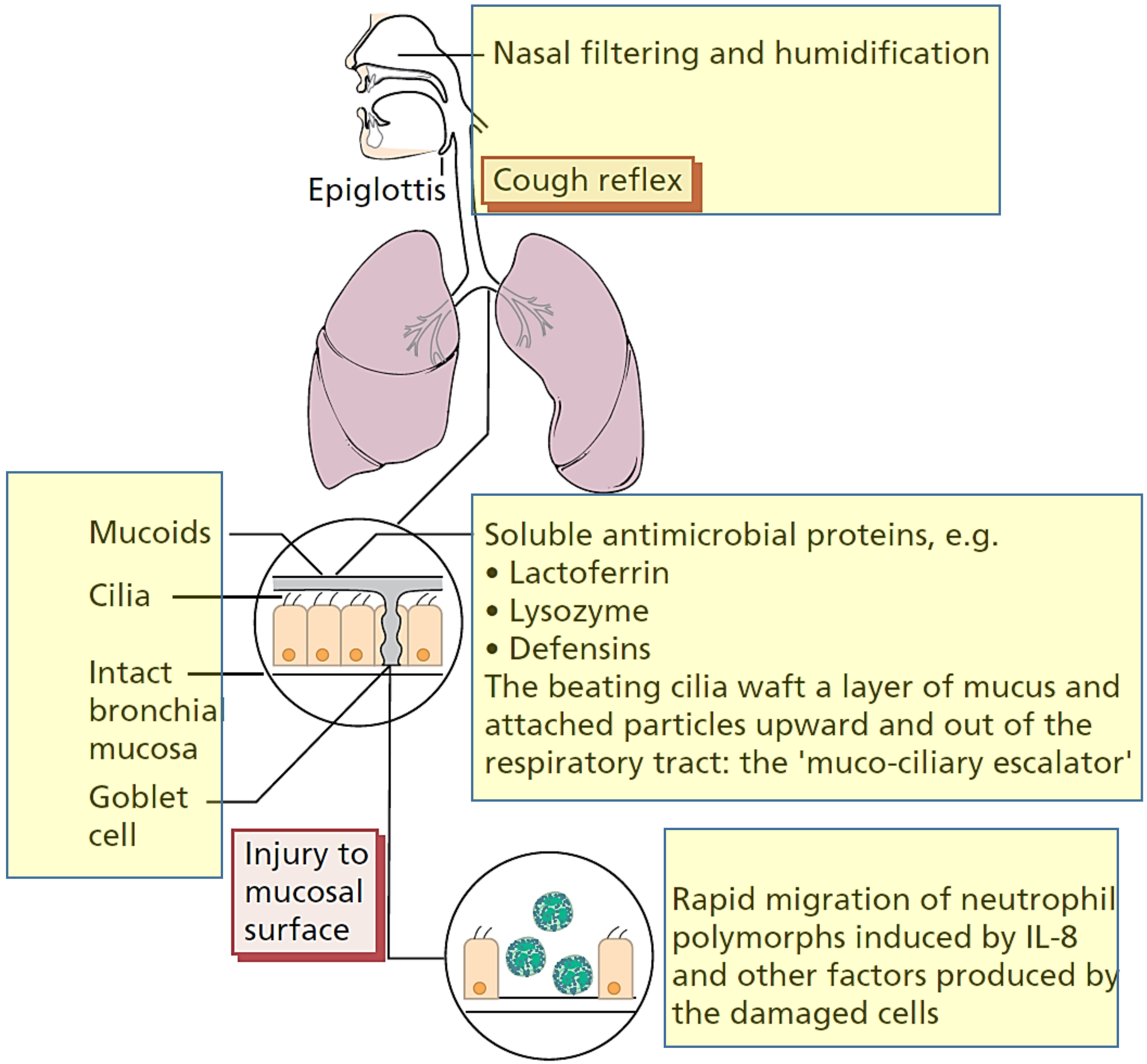


Fig. 13.1 Non-specific protective mechanisms in the airways.

رخدادهای ایمنی ذاتی (دفاع مکانیکی)

مژک ها و سطوح
Mucucilliary به دام
اندازی ارگانیسم ها و
پارتیکل

رفلکس سرفه
همکاری عضلات تنفسی
و CNS تماس پارتیکل
با پایانه های عصبی

ترشحات ضد میکروبی
موکوسی لیزوزیم ،
لاکتوفرین

اپی تلیوم تنفسی =

گرم کردن ، فیلتراسیون ،

مرطوب نمودن هوای
تنفسی

- جذب بخارهای مضر
- پوشش محکم و
چسبنده

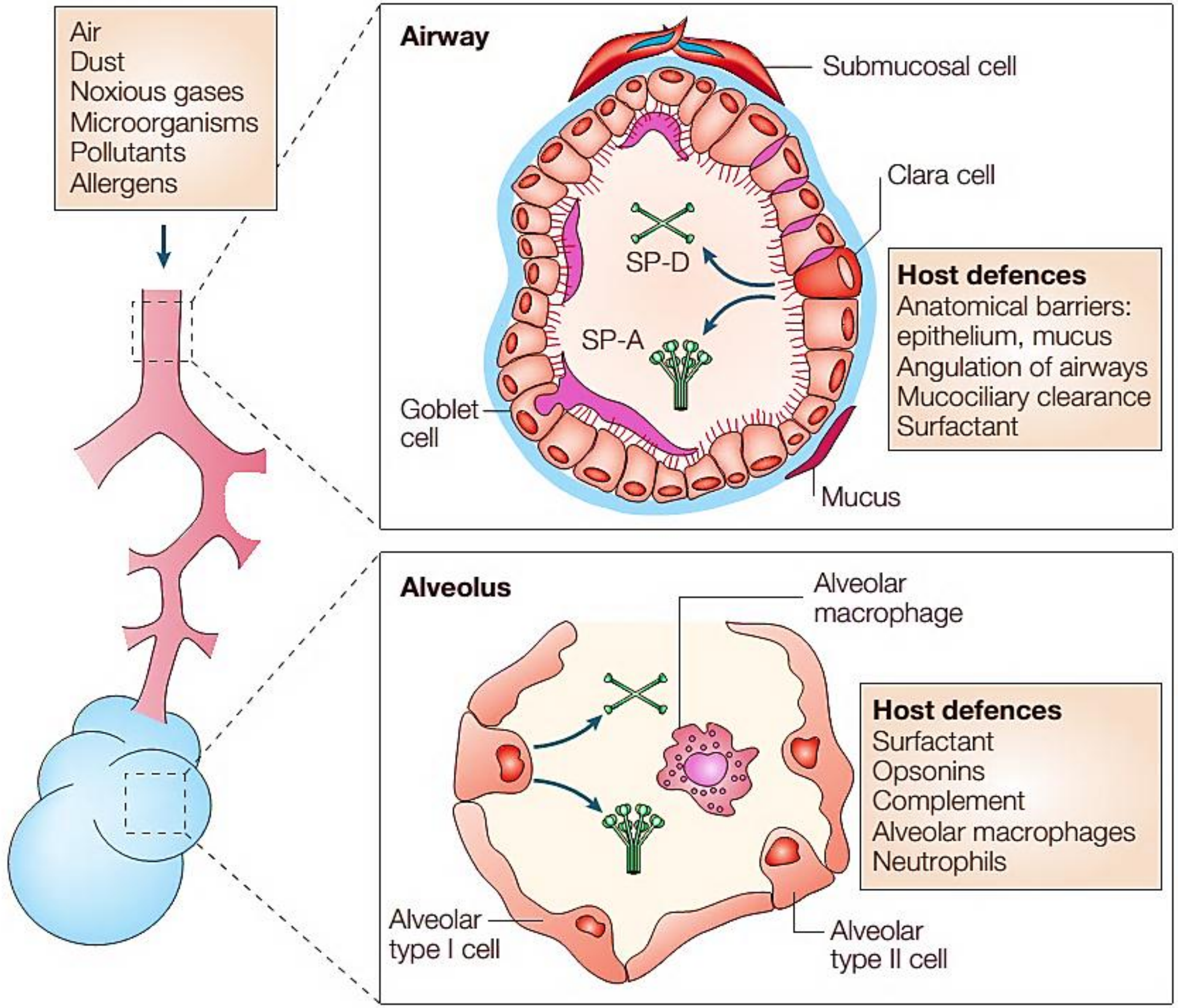
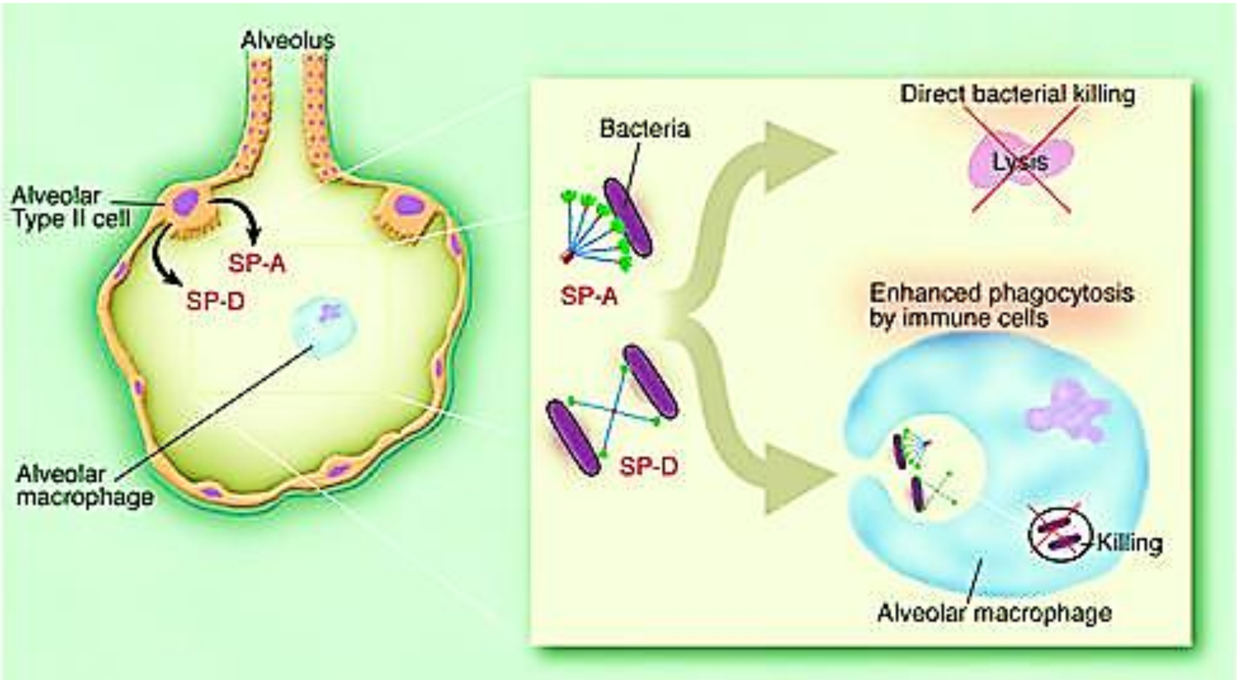


Figure 1 | **Lung host-defence mechanisms.** The lung is constantly challenged by inhaled pathogens, pollutants and particles. Several different defence mechanisms contribute to lung defence. These include filtration in the naso-oropharynx and conducting airways, sneezing, coughing and mucociliary clearance. Small particles might reach the alveolar gas-exchange regions of the lung. Host-defence functions in the peripheral air-spaces include surfactant, other opsonins (such as immunoglobulins) and innate immune cells (including alveolar macrophages and neutrophils). SP-A, surfactant protein A; SP-D, surfactant protein D.

Table 2 | **First-line defence molecules produced by airway epithelial cells (AECs)**

AEC-secreted product	Action	Refs
Mucins	Host defence; bind infectious agents	85
Surfactant protein C	Maintenance of surfactant proteins; bind infectious agents	85
Surfactant protein A and surfactant protein D (collectins)	Opsonins for pathogen clearance; direct inhibition; activate other immune cellular functions	86
Complement and complement cleavage products	Promote phagocytosis; bridging of innate and adaptive immunity; resolution and repair	87
Antimicrobial peptides (defensins, cathelicidins, histatins, lysozyme, lactoferrin, SLPI, Elafin, PLUNC and BPI)	Direct antimicrobial action; effector molecules; activation of adaptive immunity	88,89

BPI, bacterial permeability-increasing protein; PLUNC, palate, lung and nasal epithelium clones; SLPI, secretory leukoprotease inhibitor.



عملکرد سورفاکتانت ها در ایمونولوژی ریه

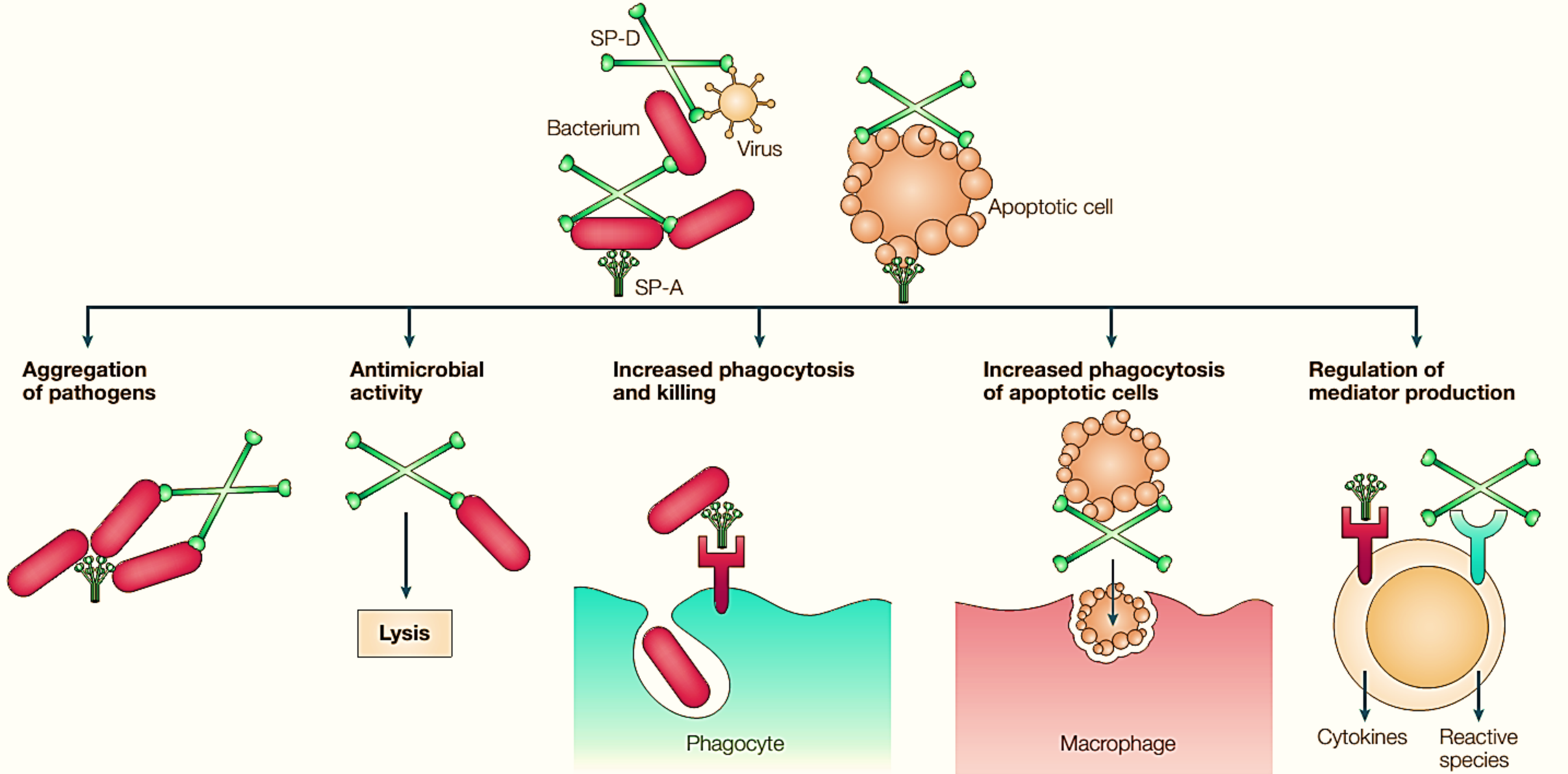


Figure 3 | **Functions of SP-A and SP-D.** Surfactant protein A (SP-A) and SP-D bind to a variety of bacteria, viruses, allergens and apoptotic cells and thereby function as opsonins to enhance the uptake of these cells and particles. Binding of the collectins to pathogens occurs by various mechanisms. Some pathogens are aggregated by SP-A and/or SP-D. SP-A and SP-D also have direct effects on immune cells and modulate the production of cytokines and inflammatory mediators.

Table 2. Humoral substances produced by airway epithelial cells upon recognition of the inhaled harmful factor

Inflammatory mediators	Chemotactic factors	Antimicrobial agents
Cytokines	LL-37/CAP-18*	B-defensins
Chemokines	β-defensins	LL-37/CAP-18*
Leukotrienes	Chemokines	Lysozyme
Calprotectin	Leukotrienes	Lactoferrin
		SPLI*
		Elafin
		Calprotectin
		Phospholipase A2
		SP-A, SP-D*
		Anionic peptides

Abbreviations: LL-37/CAP-18, Cationic antimicrobial peptides; CAP-18, Cationic antimicrobial protein-18; SLPI, secretory leukocyte proteinase inhibitor; SP, Surfactant Protein.

تشکیلات ایمنی اکتسابی (اختصاصی) در دستگاه تنفس

ایمنی سلولار
- ماکروفاژ
- دندریتیک سل
- لنفوسیت ها

ایمنی هومورال
- حضور دائم و حیاتی IgA ترشحی (مقاوم به آنزیم های پروتئولیتیک)
- IgE
- حضور ایمونوفیزیولوژیک کمپلمان

اعضای لنفاوی
- بافت لنفاوی برونشها
Bronchus-Associated Lymphoid Tissue (BALT)
- غدد لنفاوی ناف ریه
- غدد لنفاوی مدیاستینال
- لوزه ها = حلقه waldyeres

TABLE 1 Major constituents of lung defences

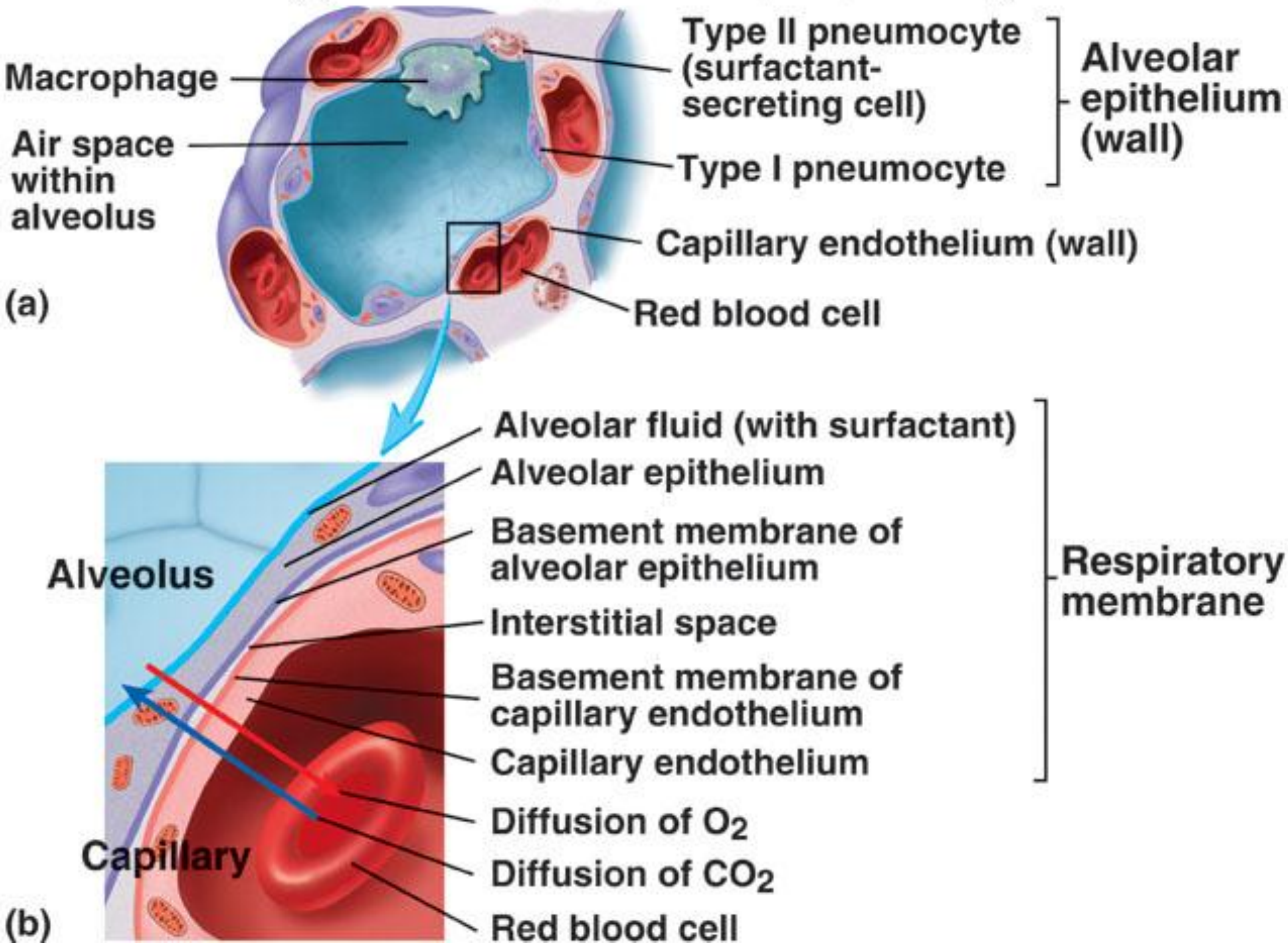
Airways and their mucosa

- Luminal defence mechanisms
  - Anatomical barrier
  - Cough
  - Mucociliary clearance
  - Secretory IgA
  - Lysozymes, lactoferrins
  - Defensins
- Epithelial cells
  - Epithelial barrier
  - Mucin release
  - Antimicrobial peptides
  - Bacterial receptors
  - Chemotactic factors
  - Growth factors; cytokines
- Blood derived cells of the mucosa
  - Dendritic cells
  - Lymphocytes (T-cells; γδ; NK cells)
  - B lymphocytes
  - Eosinophils; mast cells; basophils

Alveolar spaces

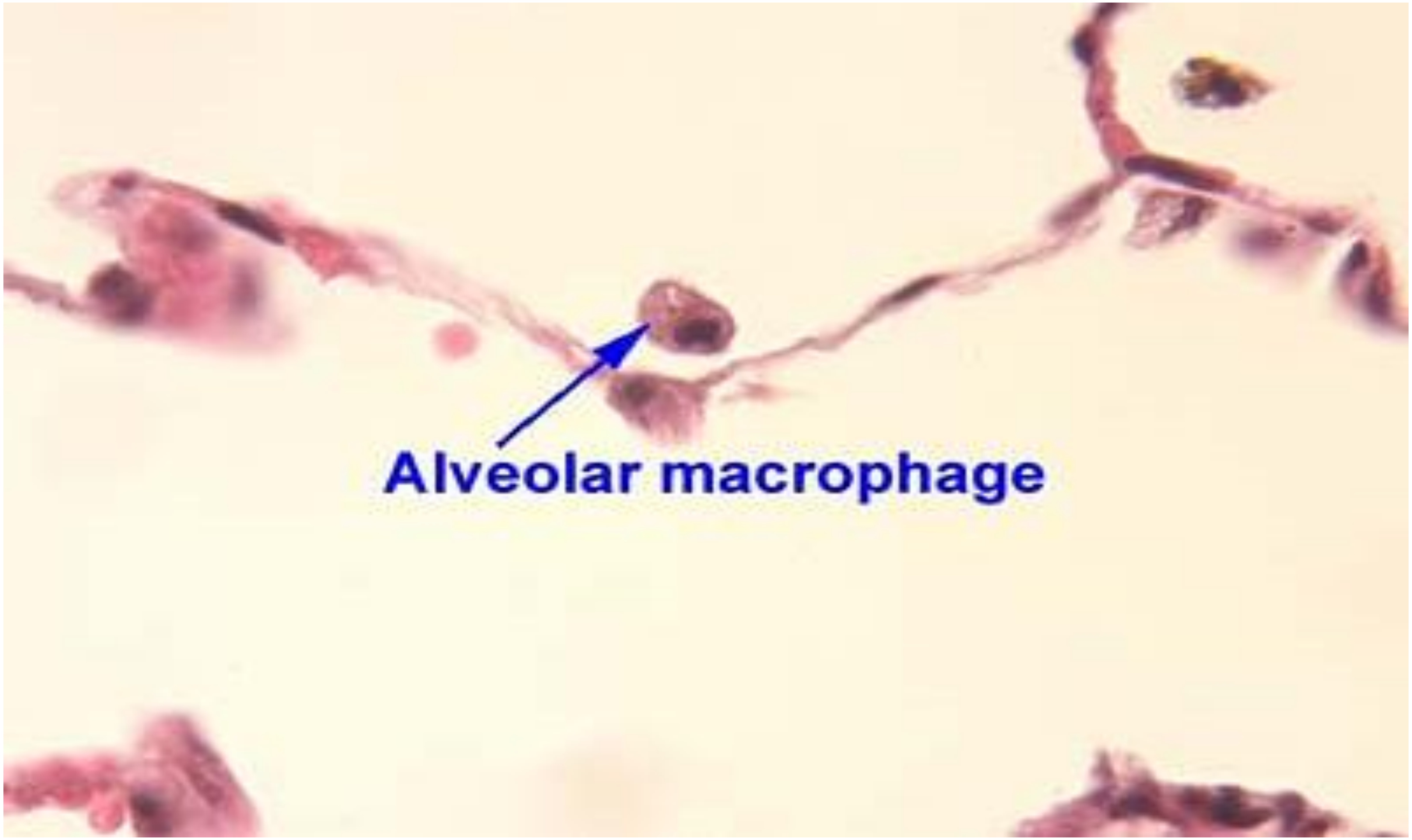
- Pneumocyte types I and II
- Alveolar macrophages
- Lymphocytes
- Neutrophils
- IgG and opsonins
- Surfactant

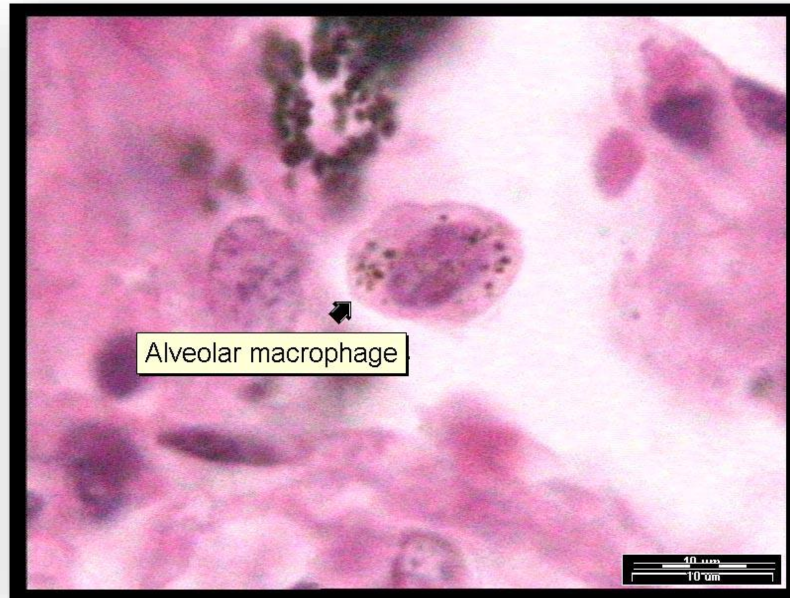
Ig: immunoglobulin; NK: natural killer.


Macrophage
Air space within alveolus
(a)
Type II pneumocyte (surfactant-secreting cell)
Type I pneumocyte
Alveolar epithelium (wall)
Capillary endothelium (wall)
Red blood cell
Alveolus
Capillary
(b)
Alveolar fluid (with surfactant)
Alveolar epithelium
Basement membrane of alveolar epithelium
Interstitial space
Basement membrane of capillary endothelium
Capillary endothelium
Respiratory membrane
Diffusion of O_2
Diffusion of CO_2
Red blood cell

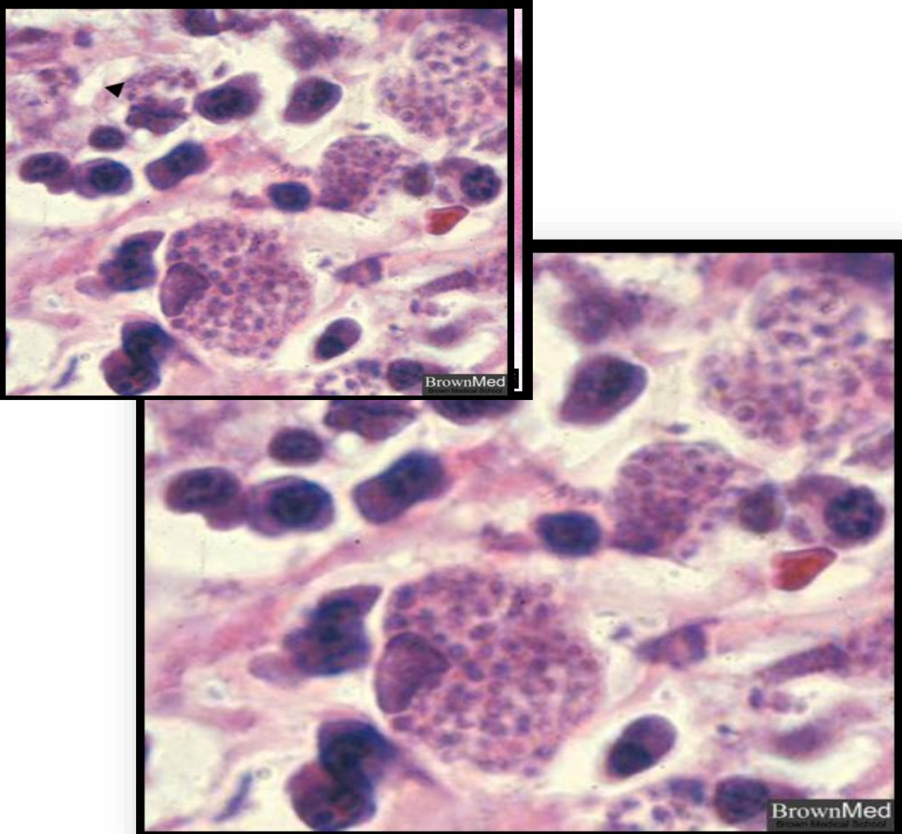
Dust cells, also known as alveolar macrophage cells, help to keep the alveoli clean of bacteria and small particulates.

Views of dust cells in the alveoli of the lungs.


Alveolar macrophage



شکل۶- ۴: ماکروفاژ آلوئولار که حاوی ذرات و پارتیکلهای بلع شده در فضای آلوئولار است.



شکل ۶-۵ : در یک عفونت شدید بافت ریوی با هیستوپلاسما کپسولاتوم (قارچ تنفسی)، ماکروفاژهای آلوئولار به شدت آلوده و انباشته از اسپور گردیدهاند. این تصویر از یک نمونه بافتی اخذ شده از بیماران مبتلا به این عفونت تهیه شده است.

ویژگی و عملکرد ماکروفاژهای آلوئولار

نام dust cell =نشان دهنده فعالیت ویژه در غبار روبی فضای آلوئولار

طول عمر بسیار

حرکت آزادانه در فضای آلوئولار- حضور دائم در دیواره بین آلوئولی

نقش تنظیمی و تحریکی سایر سلول های ایمنی

حرکت پس از فاگوسیتوز میکروب

همراهی و همکاری با سایر سلولهای بافت تنفسی ریه (فیبروبلاستها ، ماست سل ها و ائوزینوفیل ها)

تولید فاکتورهای رشد فیبروبلاستی، آنها را وادار به ترشح اجزاء بافت همبندی می‌نمایند

تولید کموکاین‌ها، سیتوکاین‌ها و اجزاء کمپلمان

پل ارتباطی قوی بین دفاع ذاتی و اختصاصی

ازعوامل مهم در مهار عفونتهای باکتریایی

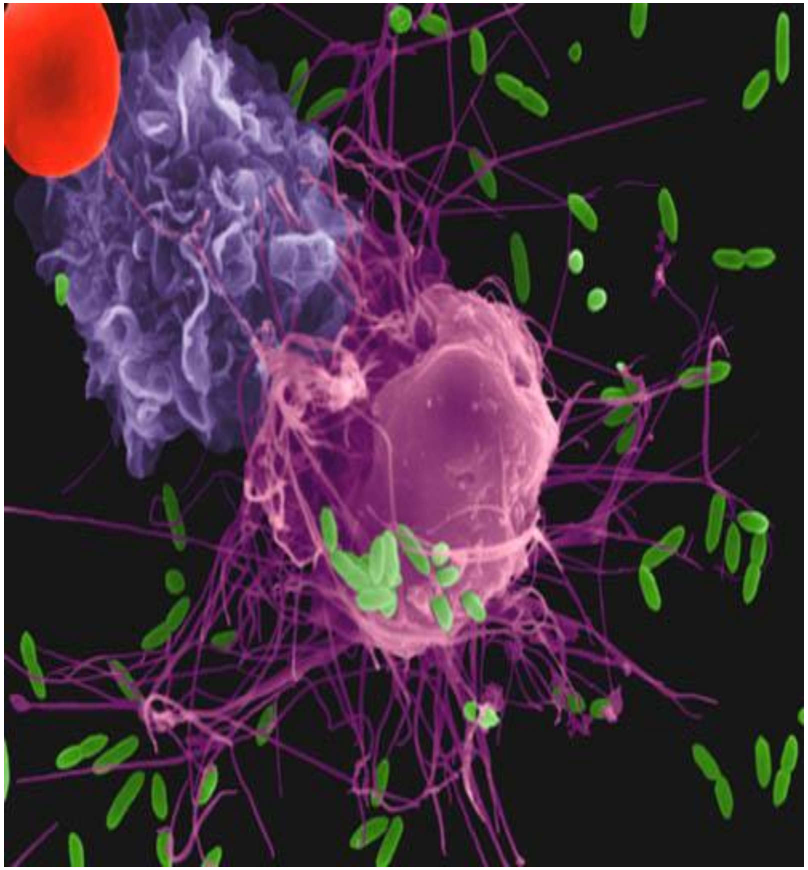
تولیدات آنتی باکتریال ماکروفاژهای آلوئولار= تولیدات اکسیداتیو (ROI ، RNOI) تولید سورفکتانت های ریوی (از گروه کولکتین ها) و تولیدات آنزیمی برای مقابله با میکروبها (اسید فسفاتاز)

اثرات سیتوتوکسیک قوی و مستقیم بر سلولهای سرطانی شده ریوی

خنثی سازی کارسینوژنهای شیمیایی از طریق بلع آنها مثلاً : آزبستوز و سیلیکا و ....

یکی از راههای دستیابی به جمعیت های سلولی این منطقه، انجام عمل لاواژ برونکوآلوئولار است که راه بسیار مناسبی برای دستیابی به سلولها و مطالعه نحوه عملکرد آنهاست.

alveolar macrophage



Sources :

- Bone marrow - monocyte - macrophage

Function :

- Phagocytosis
- Immune-regulation

  suppression - PGE2
- Immune-enhancement

  – pro-inflammatory cytokines

سرنوشت بلع پارتیکل ها توسط ماکروفاژهای آلوئولار ۱

فاگوسیتوز ← حرکت خلاف مسیر آلوئولار ← بطرف بافت بینابینی آب میان بافتی ← کانالهای لنفاوی ← جریان لنف ← غدد لنفاوی تنفسی ← ایمنی اختصاصی

- در بیماریهای عفونی مزمن، منجمله سل و عفونت‌های قارچی تنفسی، سیر اولیه حرکت ماکروفاژهای آلوده به میکروارگانیسم از نوع از این مسیر تبعیت می‌کند . سلول بلع کننده باکتری عمل حذف کامل و انهدام باکتری را به انجام نرسانده با انتخاب مسیر لنفاوی موجب ورود باکتری به اجزاء سیستم ایمنی می‌گردد.
- و بدین ترتیب با وجود احاطه گردیدن باکتری توسط سلولهای صلاحیت دار ایمنی، مسیر تکامل و گسترش عفونت سلی براحتی هموار می‌گردد.

سرنوشت بلع پارتیکل ها توسط ماکروفاژهای آلوئولار ۲

فاگوسیتوز ← جریان برعکس مورد فوق ← حرکت ماکروفاژ به سمت درخت برونشیال ← ورود به مجاری تنفسی ← تراشه لارنکس ← فارنکس ← رفلکس سرفه ← دفع پارتیکل (در کودکان بلع معدی صورت می گیرد)

- مثالی دیگر از عملکرد ماکروفاژهای آلوئولار، اختلالات قلبی- عروقی است . خونی که از عروق ریوی به دلیل ناهنجاریهای عروقی خارج می‌گردد.
- و به سمت آلوئول روانه می شود، توسط ماکروفاژهای آلوئولار بلع می‌شود و این خود راهی برای پاکسازی از وجود گلبولهای قرمز نشست شده می‌باشد.
- بطوری که ماکروفاژهای آلوئولار محتوی هموسیدرین در محتویات خلط یافت می‌شوند و توسط عمل سرفه راه خروجی را به سمت دهان طی می‌کنند.

مهاجرت سلول های ایمنی در ریه

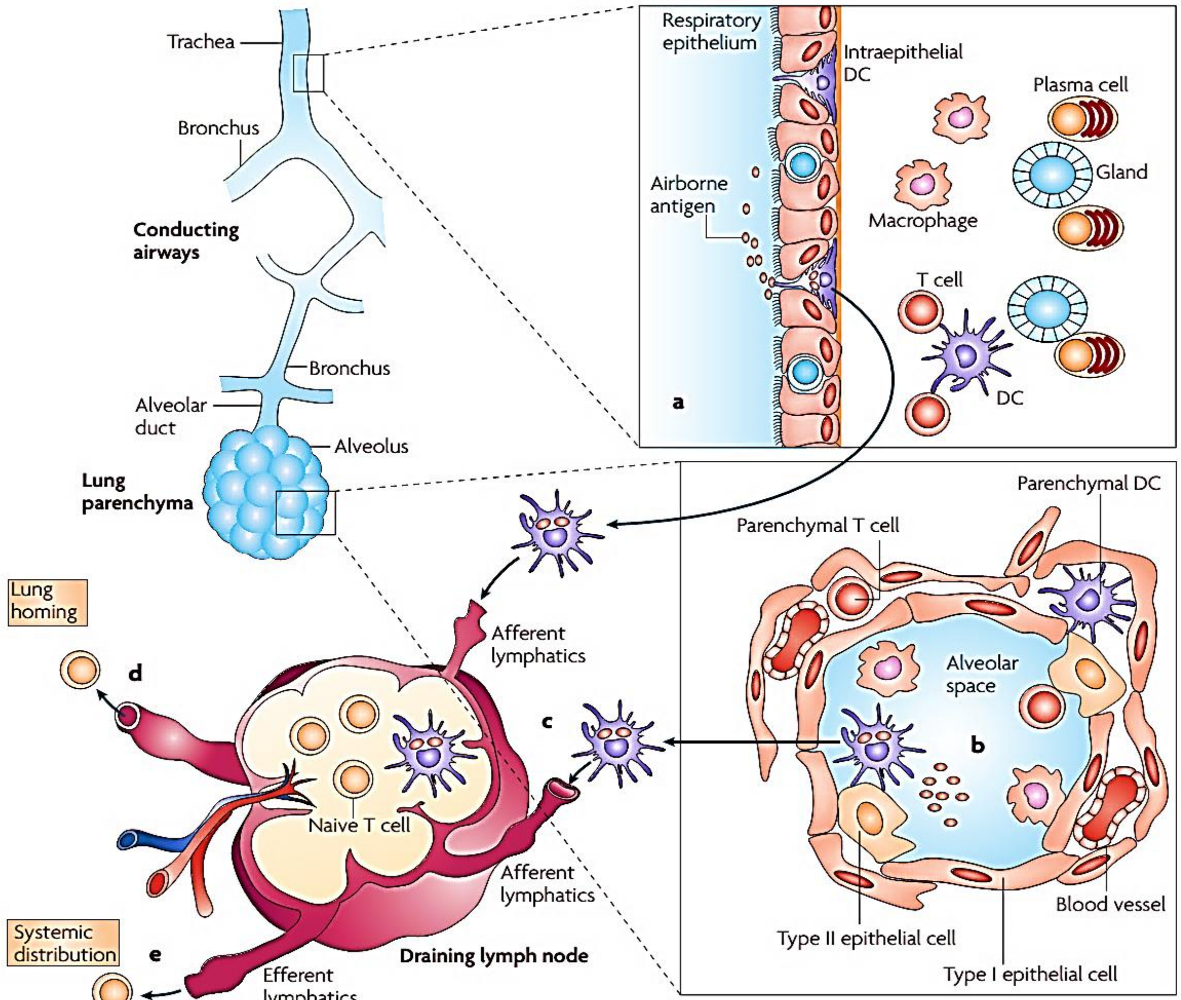
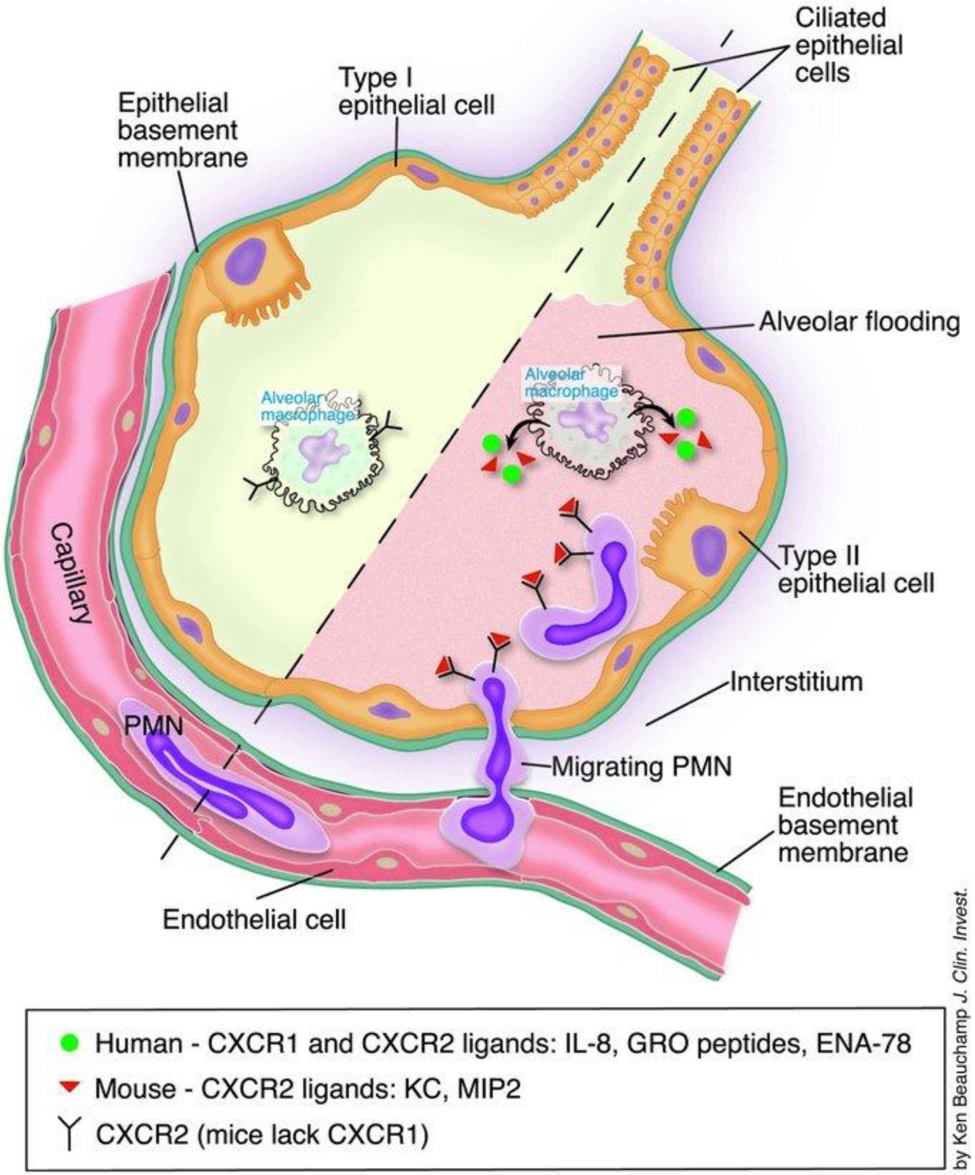


Figure 1 | **Antigen uptake and migratory patterns for immune induction in the lungs.** Local immune cells in the two lung compartments showing capture of airborne antigens and subsequent recognition by T cells in the draining lymph nodes. Luminal antigens are sampled by dendritic cells (DCs) that are located within the surface epithelium of the bronchial mucosa (**a**) or in the alveoli (**b**). Antigen-bearing DCs upregulate CC-chemokine receptor 7 and migrate through the afferent lymphatics to the draining lymph nodes and present antigenic peptides to naive antigen-specific T cells (**c**). Activated T cells proliferate and migrate through the efferent lymphatics and into the blood via the thoracic duct. Depending on their tissue-homing receptor profile, effector T cells will exit into the bronchial mucosa through postcapillary venules in the lamina propria or through the pulmonary capillaries in the lung parenchyma (**d**), or disseminate from the bloodstream throughout the peripheral immune system (for example, to other mucosal sites) (**e**).



در هنگام نیاز و مواجهه با عوامل عفونی ماکروفاژهای آلوئولار کموکاین می‌سازند و سلولهای بیگانه‌خوار چند هسته‌ای (نوتروفیل‌ها) به دلیل دارا بودن گیرنده برای کموکاین‌ها، در همکاری با آنها به فضای آلوئولار مهاجرت می‌کنند و این سرآغاز التهاب در این مجموعه است.

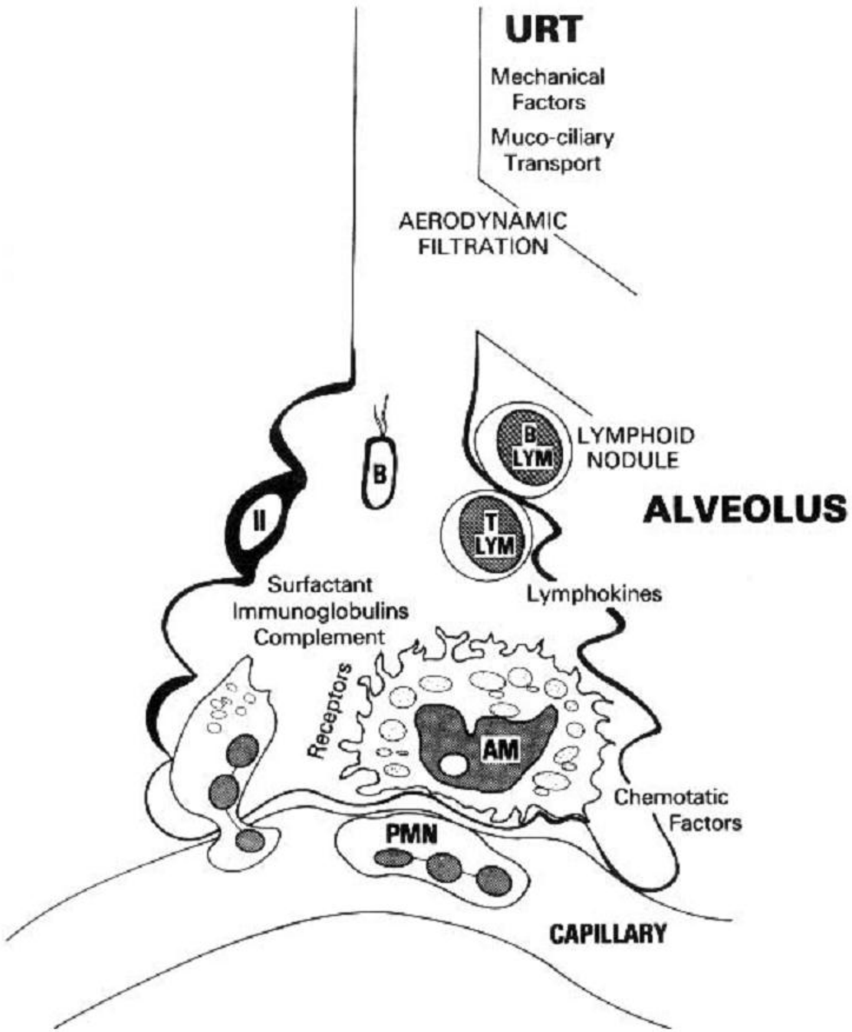


Fig. 2. Factors responsible for clearance of bacteria (B) inhaled into the lungs are quite different in the upper respiratory tract (URT) and in the lower respiratory tract, herein represented by enlargement of an alveolus. A bacterium of critical size that escapes mechanical removal from the URT and is deposited in an alveolus may encounter surfactant (secreted by type II epithelial cells) and/or immunoglobulins (antibodies) [secreted by B-lymphocytes (B LYM) or plasma

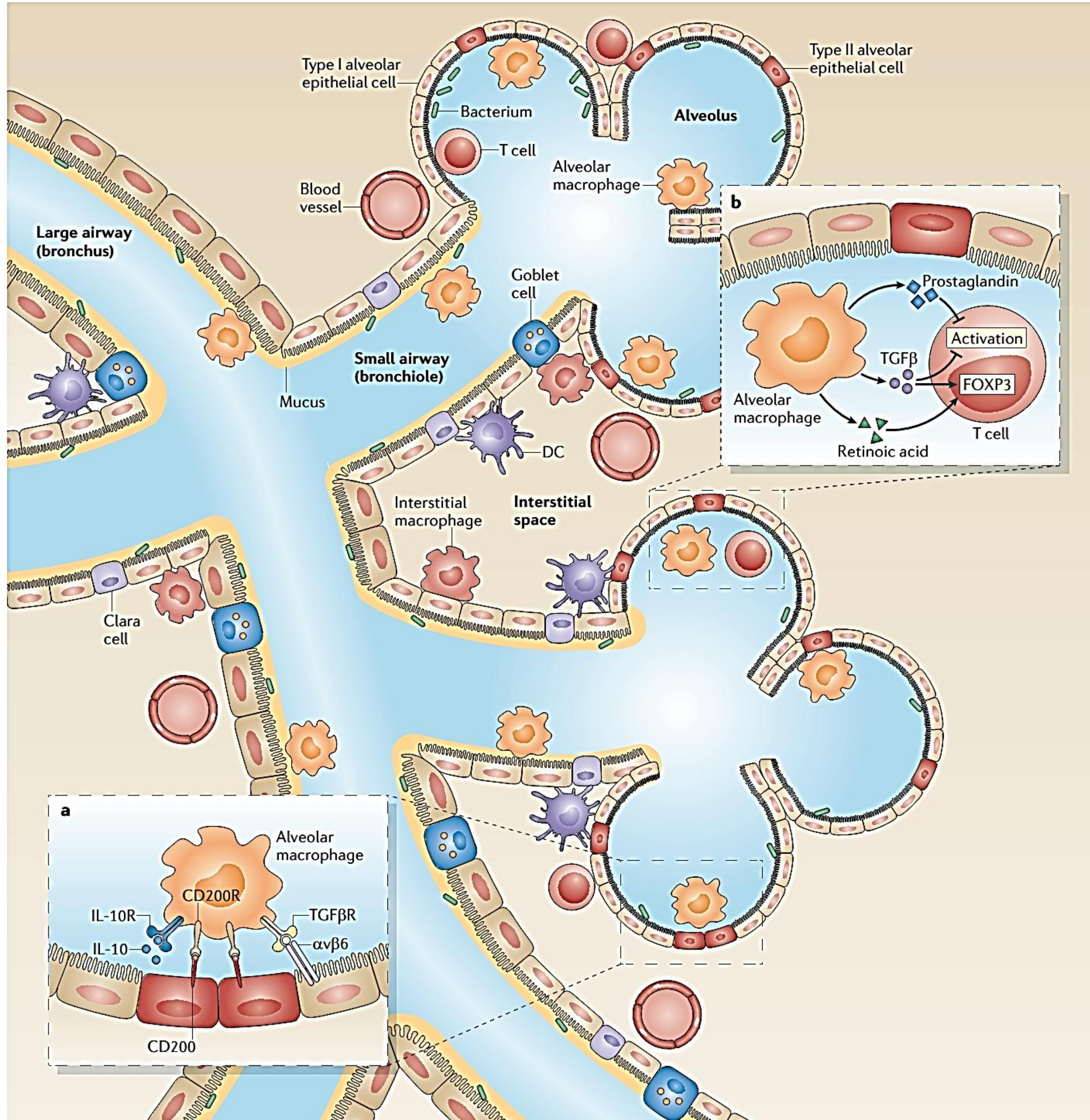
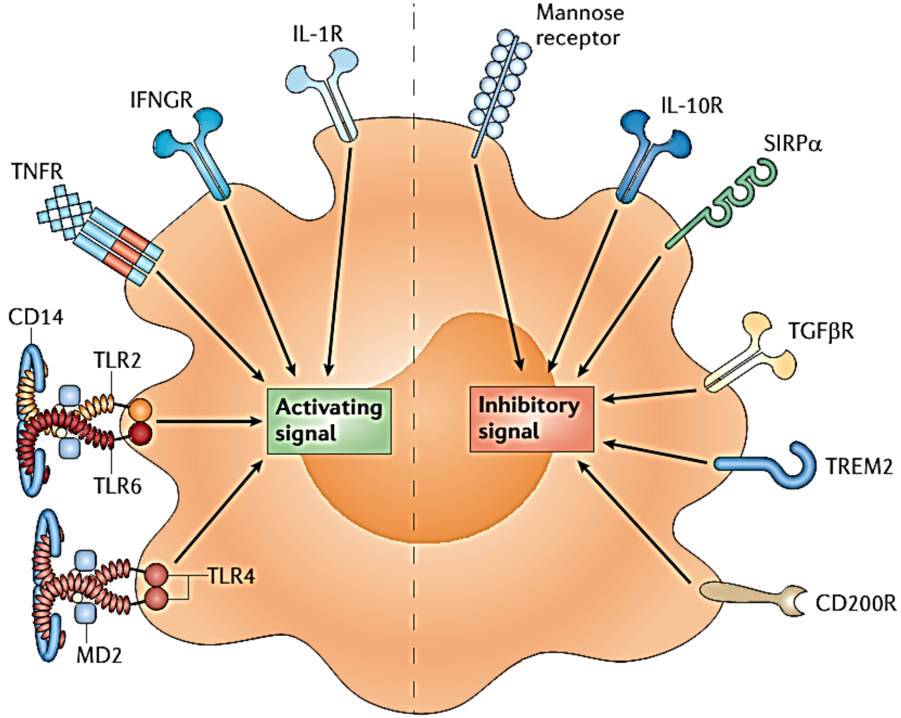


Figure 1 | **Leukocyte interactions in the healthy lungs.** Alveolar macrophages reside in the airspaces juxtaposed with type I alveolar epithelial cells (which account for as much as 98% of the total surface area of the lungs[157]) or with type II alveolar epithelial cells. Macrophages found in the larger airways (also referred to in this Review as alveolar macrophages) reside within the mucous layer. Mucus-producing goblet cells are present in both large and small airways, and secretory non-ciliated Clara cells are more common in the bronchioles[158]. Macrophages are also found in the interstitial space between the alveoli and the blood vessels where T cells, dendritic cells (DCs) and a sparse population of B cells also reside. Commensal (and pathogenic) bacteria reside within the airway mucosa and in the alveoli. **a** | Alveolar macrophages are regulated by the airway epithelium through their interactions with CD200, which is expressed by type II alveolar cells, with transforming growth factor-β (TGFβ), which is tethered to the epithelial cell surface by αvβ6 integrin, and with secreted interleukin-10 (IL-10). These interactions can also take place in the larger airways, where CD200 and αvβ6 integrin are also expressed by the bronchial epithelium. **b** | The secretion of TGFβ and retinoic acid by alveolar macrophages can induce forkhead box P3 (FOXP3) expression in both naive and activated $CD4^+$ T cells that are present in the lumen of the airways. In addition, TGFβ and prostaglandins suppress T cell activation. CD200R, CD200 receptor; IL-10R, IL-10 receptor; TGFβR, TGFβ receptor.



Alveolar macrophage

Figure 3 | **The balancing act of macrophage activation.** Alveolar macrophage activation and the initiation of inflammation involves a complex balancing act between activating and repressing signals. On the one hand, Toll-like receptors (TLRs), along with their co-receptors such as MD2 and CD14, recognize pathogen-associated molecular patterns and receptors for inflammatory cytokines, such as tumour necrosis factor (TNF), interleukin-1β (IL-1β) and interferon-γ, which perpetuate inflammation. On the other hand, mediators such as IL-10 and soluble or αvβ6 integrin-tethered transforming growth factor-β (TGFβ) block pathways that lead to inflammation. Cell–cell interactions with bronchial or alveolar epithelial cells also deliver inhibitory signals to alveolar macrophages, for example, through CD200 receptor (CD200R), triggering receptor expressed by myeloid cells 2 (TREM2) or signal-regulatory protein-α (SIRPα). Loss of the ligands for the negative regulators, for example, following epithelial cell loss during inflammation, will tip the balance towards alveolar macrophage activation. Conversely, increased expression of the negative regulators and inhibition of TLR signalling pathways, for example, in the resolution of inflammation, tips the balance towards the repression of alveolar macrophages. IFNGR, interferon-γ receptor; IL-1R, IL-1 receptor; TGFβR, TGFβ receptor; TNFR, TNF receptor.

سلول های دندریتیک در ریه

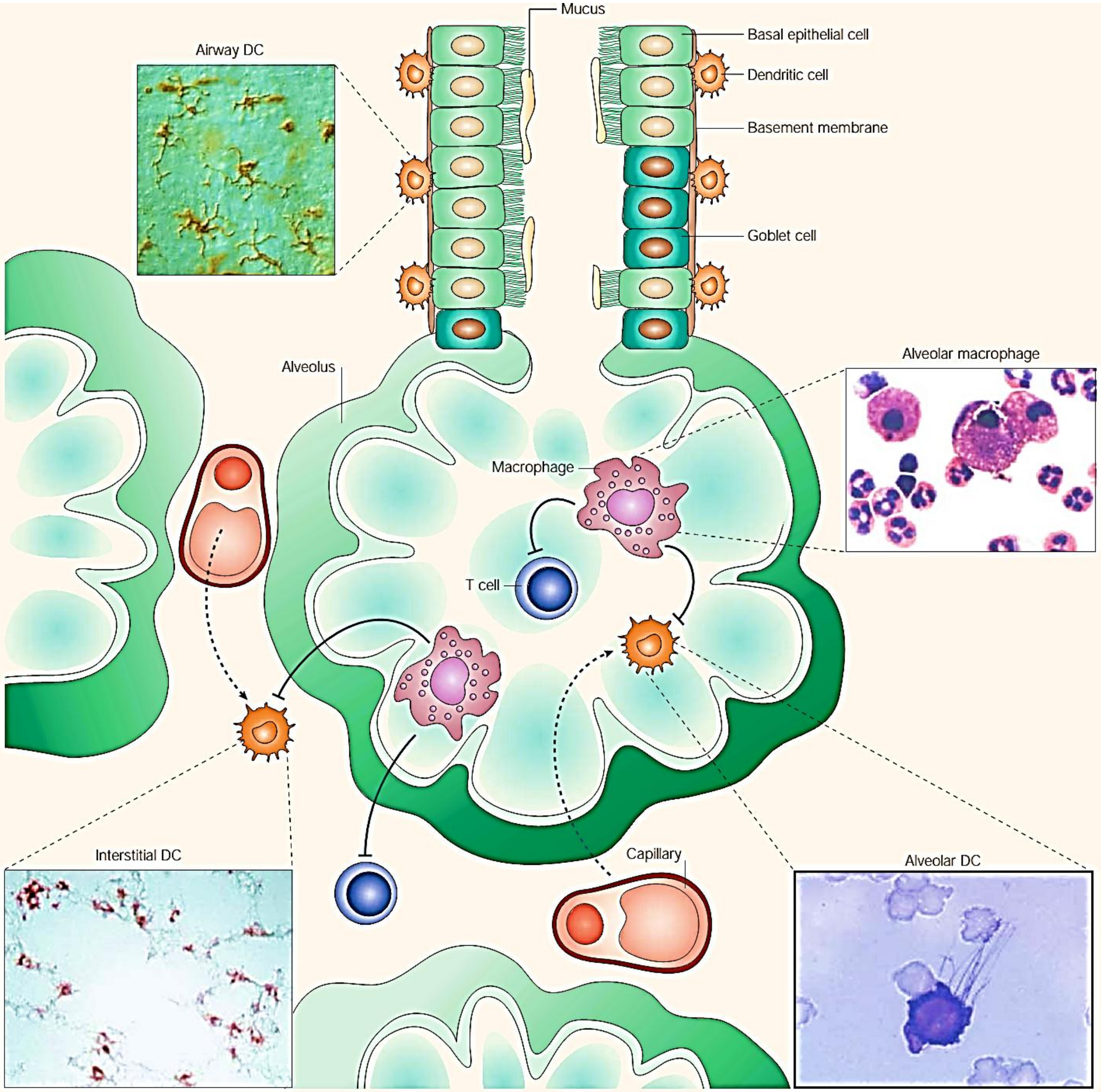


Figure 1 | **Distribution of dendritic cells in the lungs.** Airway dendritic cells (DCs) are located as a network immediately above and beneath the basement membrane, in between basal epithelial cells. Interstitial DCs (stained for CD11c) are composed of a $B220^{+}Gr\text{-}1^{+}$ plasmacytoid DC subset and a $B220^{-}$ myeloid DC subset. Their function can be suppressed by alveolar macrophages. Alveolar DCs can consistently be recovered by bronchoalveolar lavage in humans, rats and mice, particularly when inflammation is induced. The function of these cells can similarly be suppressed by alveolar macrophages. Alveolar macrophages can also directly suppress the function of T cells that are found in large numbers in the lung interstitium and alveolar compartment. Images reproduced from REF. 7 with permission from American Association of Immunologists © 2003.

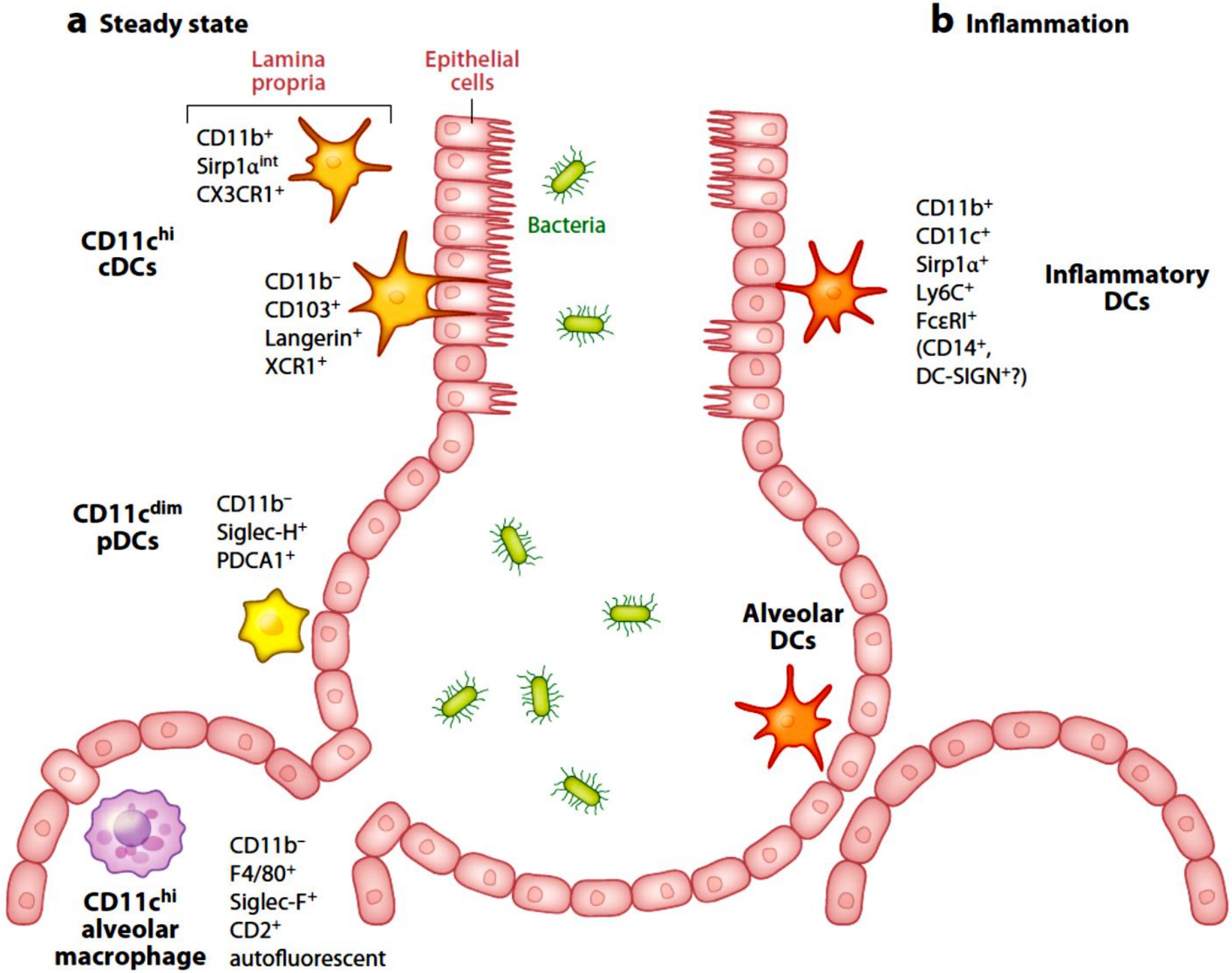
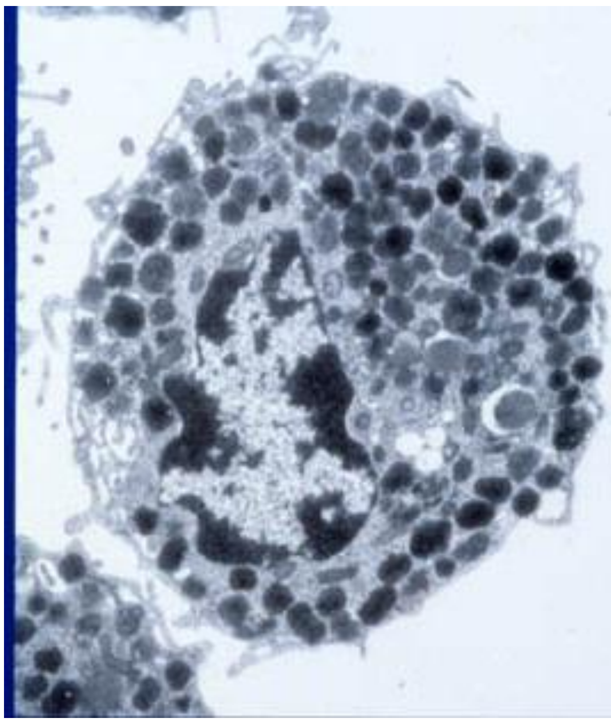


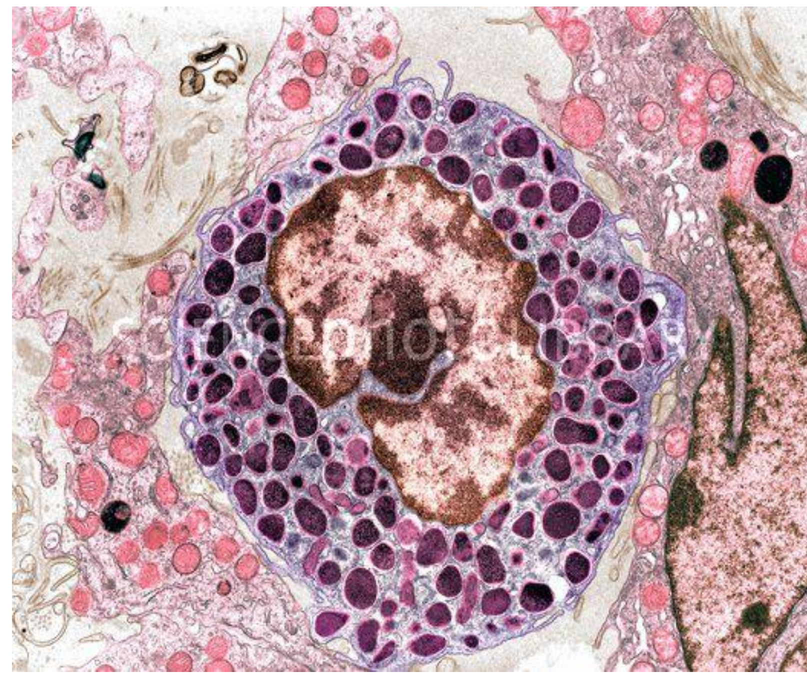
Figure 2

Different dendritic cell (DC) subsets are present in the lungs of mice. In the absence of inflammation (*a*), the lung contains two subsets of $CD11c^{hi}$ conventional (c)DCs ($CD11b^{+}$ in the lamina propria and $CD11b^{-}$ in the epithelial layer). A population of $CD11c^{dim}$ plasmacytoid (p)DCs can also be found in the conducting airways. During inflammation (*b*), additional $CD11b^{+}$ monocyte-derived DCs, expressing Ly6C and FcεRI, are recruited to the lungs.

Annu. Rev. Immunol. 2012.30:243-270.

mast cells in lung tissue



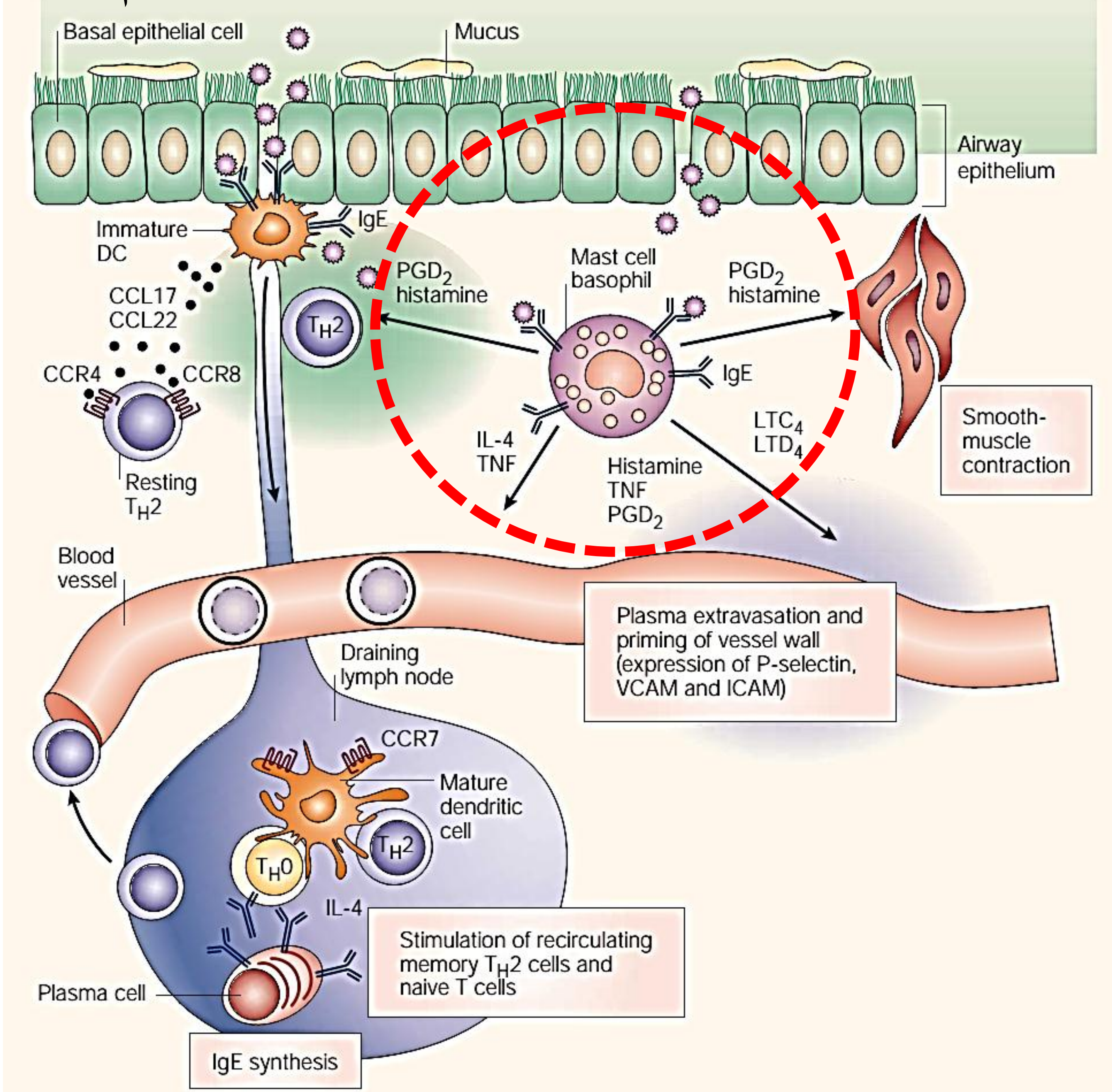


mast cells

- **protect against bacterial infection**
  - Mast cell produce TNFalpha on contact with bacterial fimbriae *(Klebsiella pneumoniae)*
  - TNF stimulates recruitment of neutrophils and macrophages which engulf bacteria.

- ***Allergy and asthma***
  - Activated mast cells immediately release preformed, granule associated inflammatory mediators (including histamine, proteases, and heparin) and are induced to generate lipid mediators (such as leukotrienes and prostaglandins), chemokines, cytokines, and
  - growth factors

نقش ماست سل و دندریتیک سل در ایجاد آلرژی و آسم در ریه



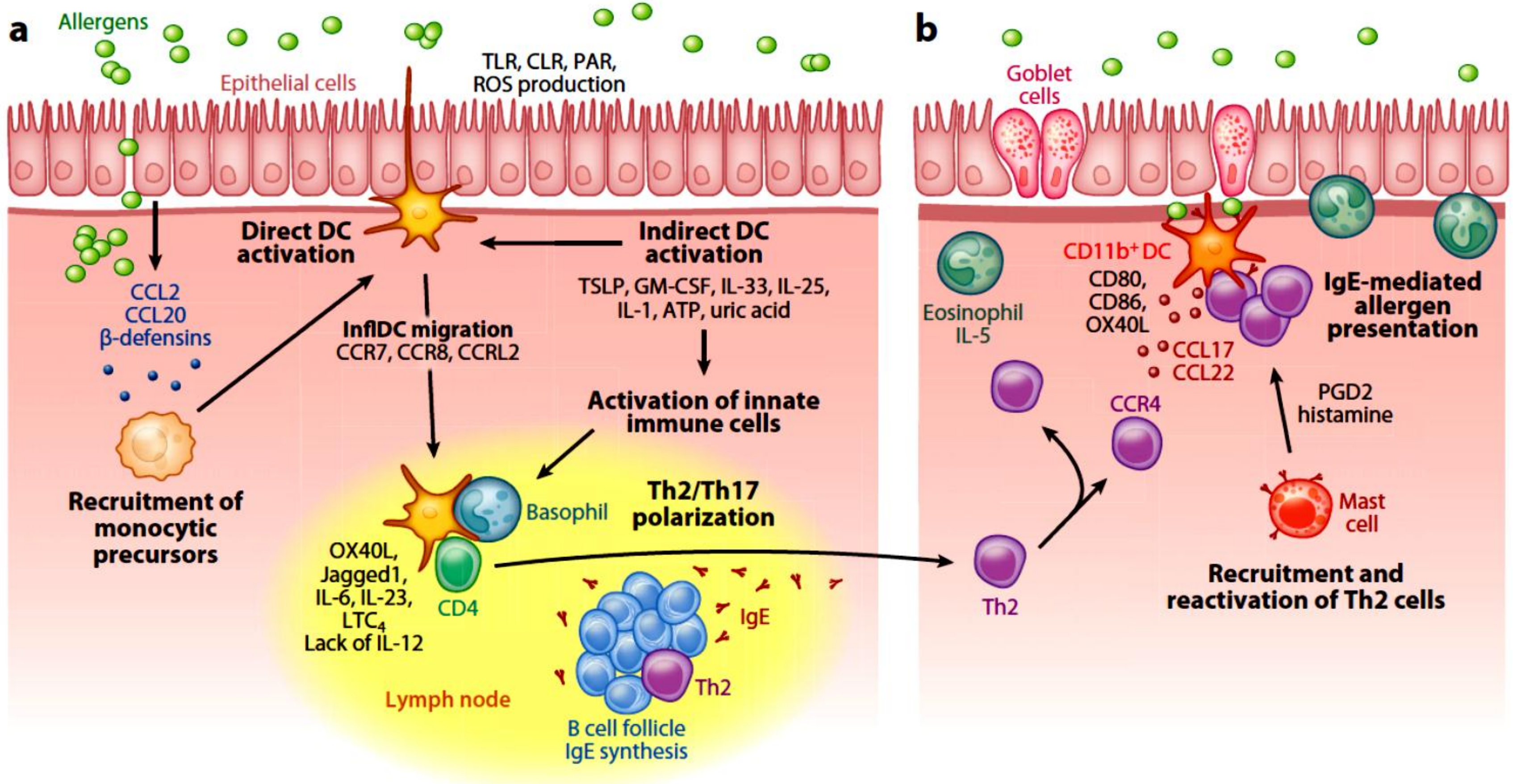
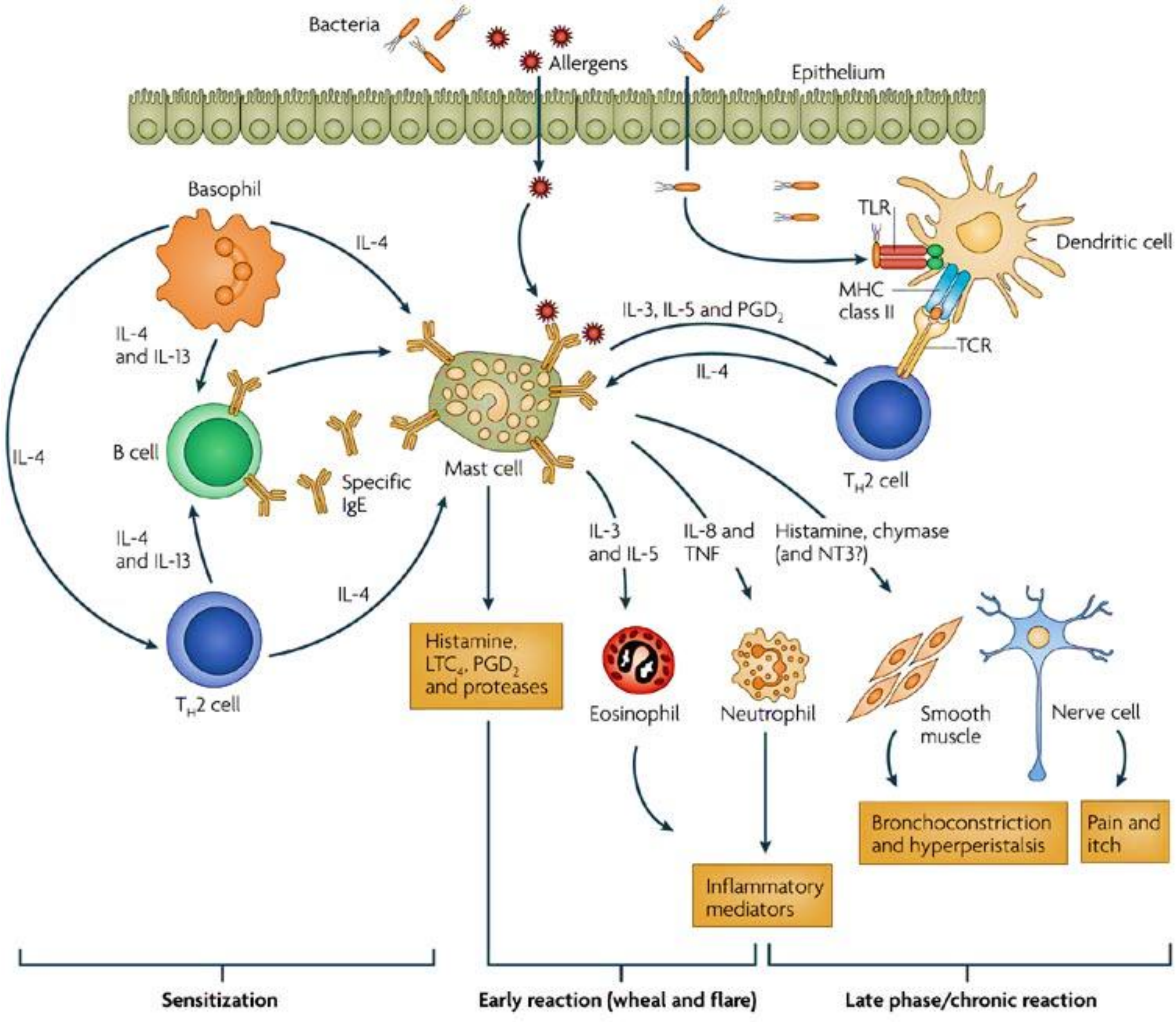


Figure 3

Both lung dendritic cells (DCs) and epithelial cells express pattern-recognition receptors (PRRs) and can be activated directly by allergens. (*a*) In response to allergens, lung epithelial cells produce chemokines that attract immature conventional (c)DCs and inflammatory monocytes (CCL2, CCL20). Activated epithelial cells produce instructing cytokines (e.g., IL-1, GM-CSF, and TSLP) and danger signals (ATP, uric acid) that favor DC maturation. Activated lung DCs then migrate to the draining mediastinal lymph nodes, where they induce Th2 and Th17 responses. DCs receive help from basophils to sustain Th2 responses. DCs also play a predominant role during the Th2 effector phase of asthma, when the lung is repeatedly exposed to allergens (*b*). During allergen challenge, DCs could locally restimulate effector function in lung-resident lymphocytes or they could recruit effector Th2 cells through CCL17 and CCL22 production. IgE-mediated allergen recognition enhances Th2 responses to inhaled allergens.


Bacteria
Allergens
Epithelium
Basophil
IL-4
TLR
Dendritic cell
MHC class II
IL-3, IL-5 and PGD_2
TCR
IL-4
and IL-13
IL-4
B cell
Specific IgE
Mast cell
T_H2 cell
IL-4
and IL-13
IL-3
and IL-5
IL-8 and TNF
Histamine, chymase (and NT3?)
IL-4
Histamine, LTC_4, PGD_2 and proteases
Eosinophil
Neutrophil
Smooth muscle
Nerve cell
T_H2 cell
Bronchoconstriction and hyperperistalsis
Pain and itch
Inflammatory mediators
Sensitization
Early reaction (wheal and flare)
Late phase/chronic reaction
Nature Reviews | Immunology

نقش ماست سل و دندریتیک سل در ایجاد آلرژی و آسم در ریه

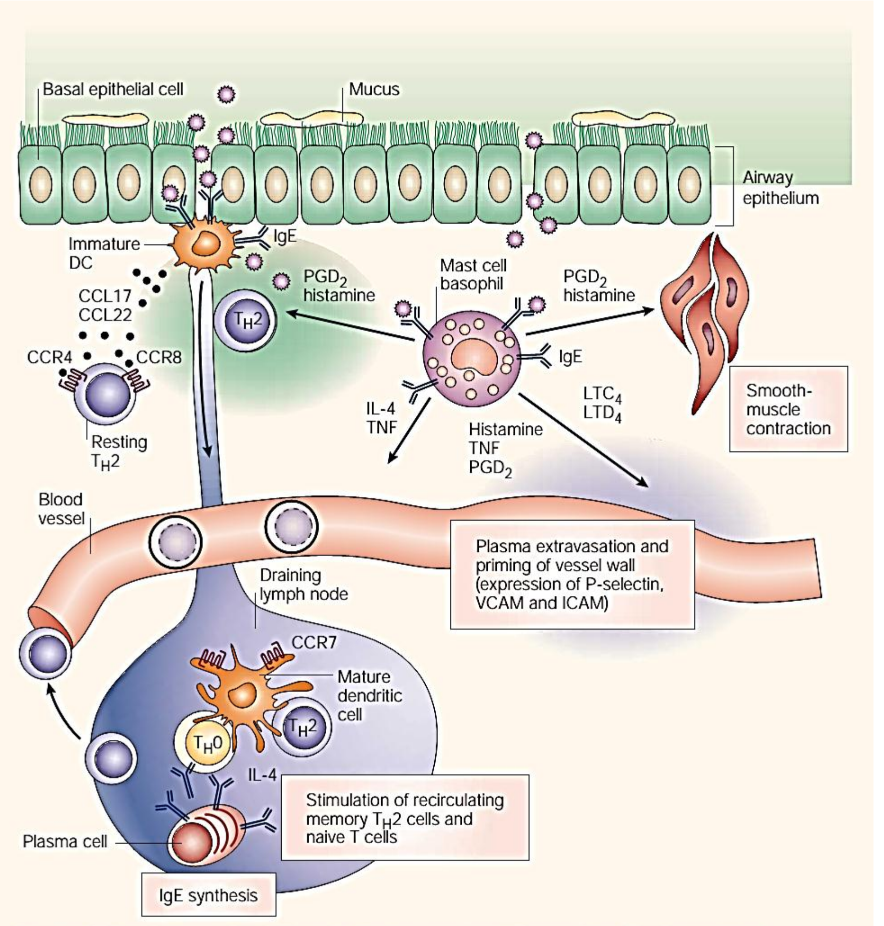


Figure 4 | **Role of airway dendritic cells during ongoing inflammation.** The first cells that recognize allergen are dendritic cells (DCs), epithelial cells and mast cells. These cells can all bind allergen-specific IgE either through FcεRI or CD23, possibly enhancing recognition of the allergen. The allergens induce the release of prostaglandins (such as prostaglandin D_2, PGD_2), leukotrienes (LTC_4 and LTD_4), histamine, chemokines (such as CC-chemokine ligand 17, CCL17 and CCL22), cytokines (such as interleukin-4, IL-4 and tumour-necrosis factor, TNF), neuropeptides and complement-breakdown products, which attract circulating DCs to the mucosa and influence DC function. Together, these mediators also induce smooth-muscle contraction, goblet-cell hyperplasia and changes to the vessel wall. In the case of house dust mite allergens, the epithelium releases granulocyte–macrophage colony-stimulating factor (GM-CSF), leading to local activation of DC function. At the same time, the Der p1 allergen activates DCs to produce CCL17 and CCL22, leading to the local attraction of T helper 2 (T_H2) cells that express CC-chemokine receptor 4 (CCR4) and possibly CCR8. Both processes occur preferentially in house dust mite atopics, but not in non-atopic individuals. The attracted T_H2 cells can directly mediate their effector function when activated by antigen-presenting cells (APCs), but fail to proliferate locally. The allergen also induces the migration of allergen-loaded DCs to the draining lymph nodes by increased expression of CCR7, which is required for homing to the T-cell area. In these areas, DCs attract recirculating resting central memory T_H2 cells and possibly some naive allergen-specific T cells, inducing their proliferation and further differentiation to T_H2 cells. Effector T_H2 cells are generated that are biased to migrate to the inflamed lung tissue, in which they collaborate with locally activated T_H2 cells to orchestrate eosinophilic inflammation. ICAM, intercellular adhesion molecule; VCAM, vascular-cell adhesion molecule.

فعال شدن ماست سل

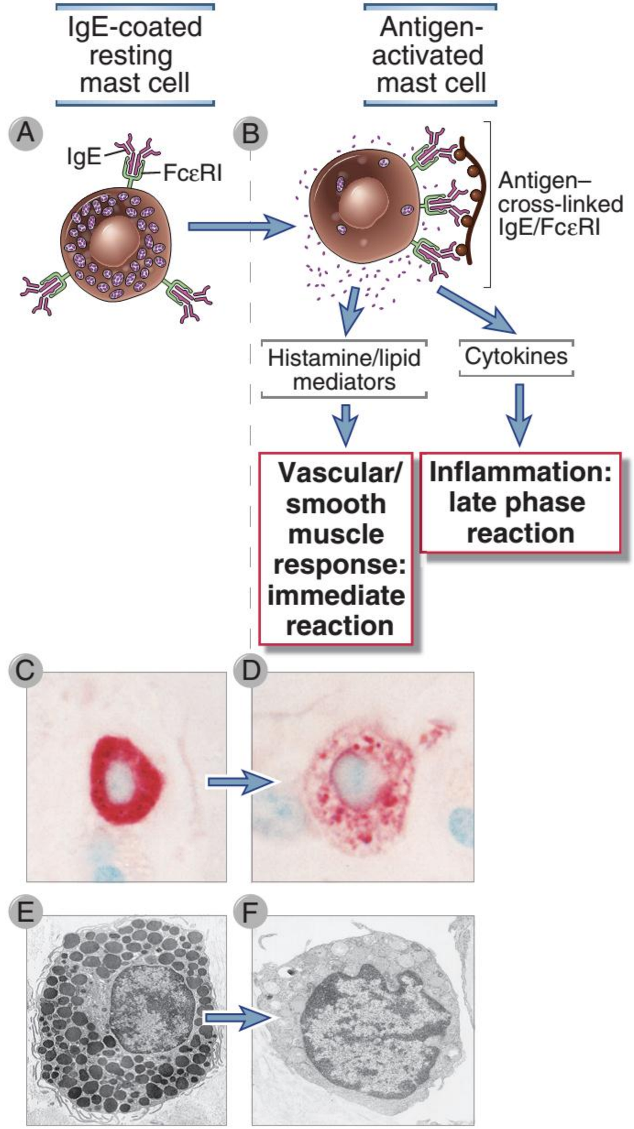


FIGURE 19–4 Mast cell activation. Antigen binding to IgE cross-links FcεRI molecules on mast cells, which induces the release of mediators that cause the hypersensitivity reaction **(A, B)**. Other stimuli, including the complement fragment C5a, can also activate mast cells. A light photomicrograph of a resting mast cell with abundant purple-staining cytoplasmic granules is shown in **C**. These granules are also seen in the electron micrograph of a resting mast cell shown in **E**. In contrast, the depleted granules of an activated mast cell are shown in the light photomicrograph **(D)** and electron micrograph **(F)**. *(Courtesy of Dr. Daniel Friend, Department of Pathology, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts.)*

واکنشهای ازدیاد حساسیت فوری

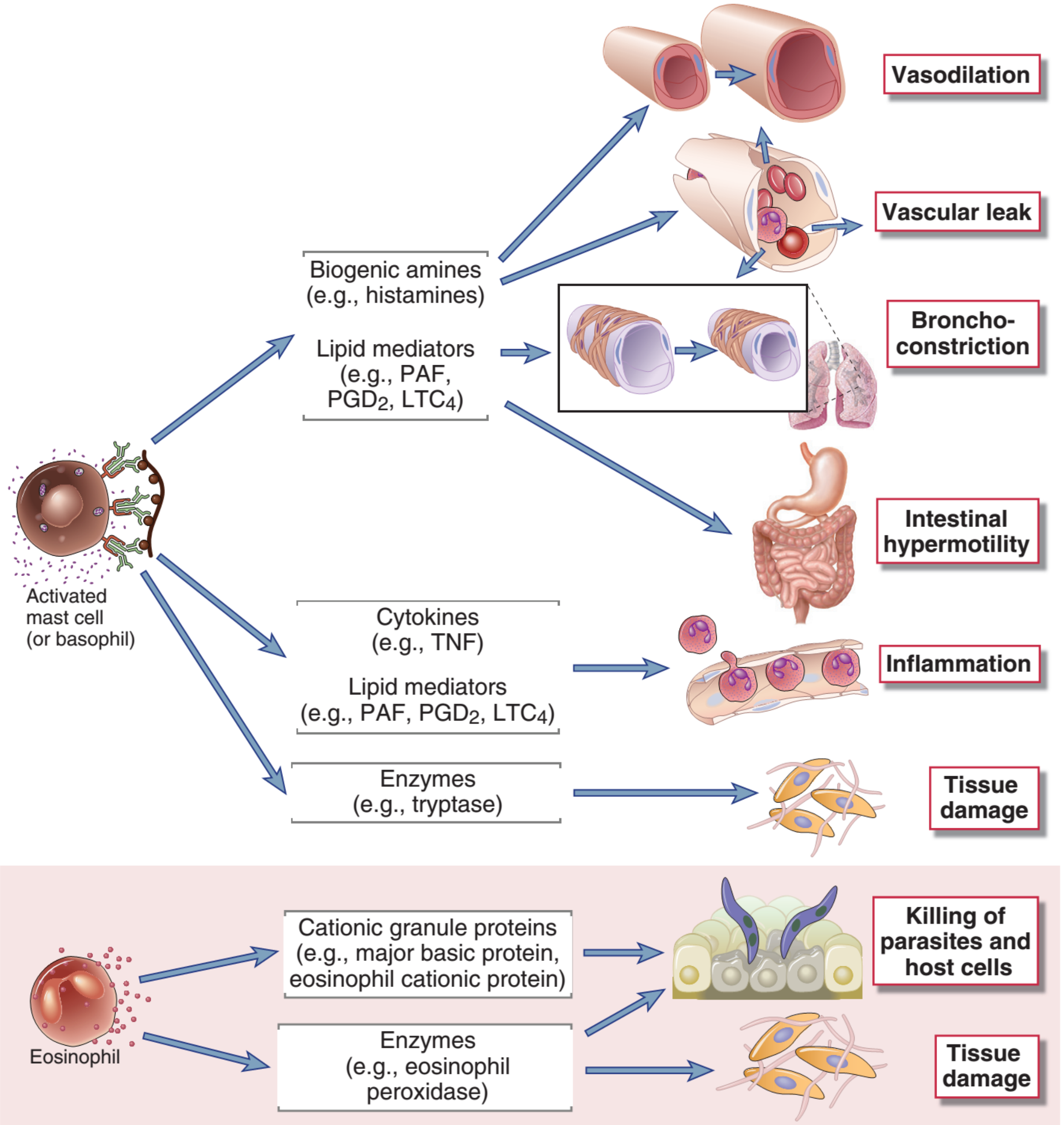


FIGURE 19–6 Biologic effects of mediators of immediate hypersensitivity. Mast cells and basophil mediators include biogenic amines and enzymes stored preformed in granules as well as cytokines and lipid mediators, which are largely newly synthesized on cell activation. The biogenic amines and lipid mediators induce vascular leakage, bronchoconstriction, and intestinal hypermotility, all components of the immediate response. Cytokines and lipid mediators contribute to inflammation, which is part of the late-phase reaction. Enzymes probably contribute to tissue damage. Activated eosinophils release preformed cationic proteins as well as enzymes that are toxic to parasites and host cells. Some eosinophil granule enzymes probably contribute to tissue damage in chronic allergic diseases.

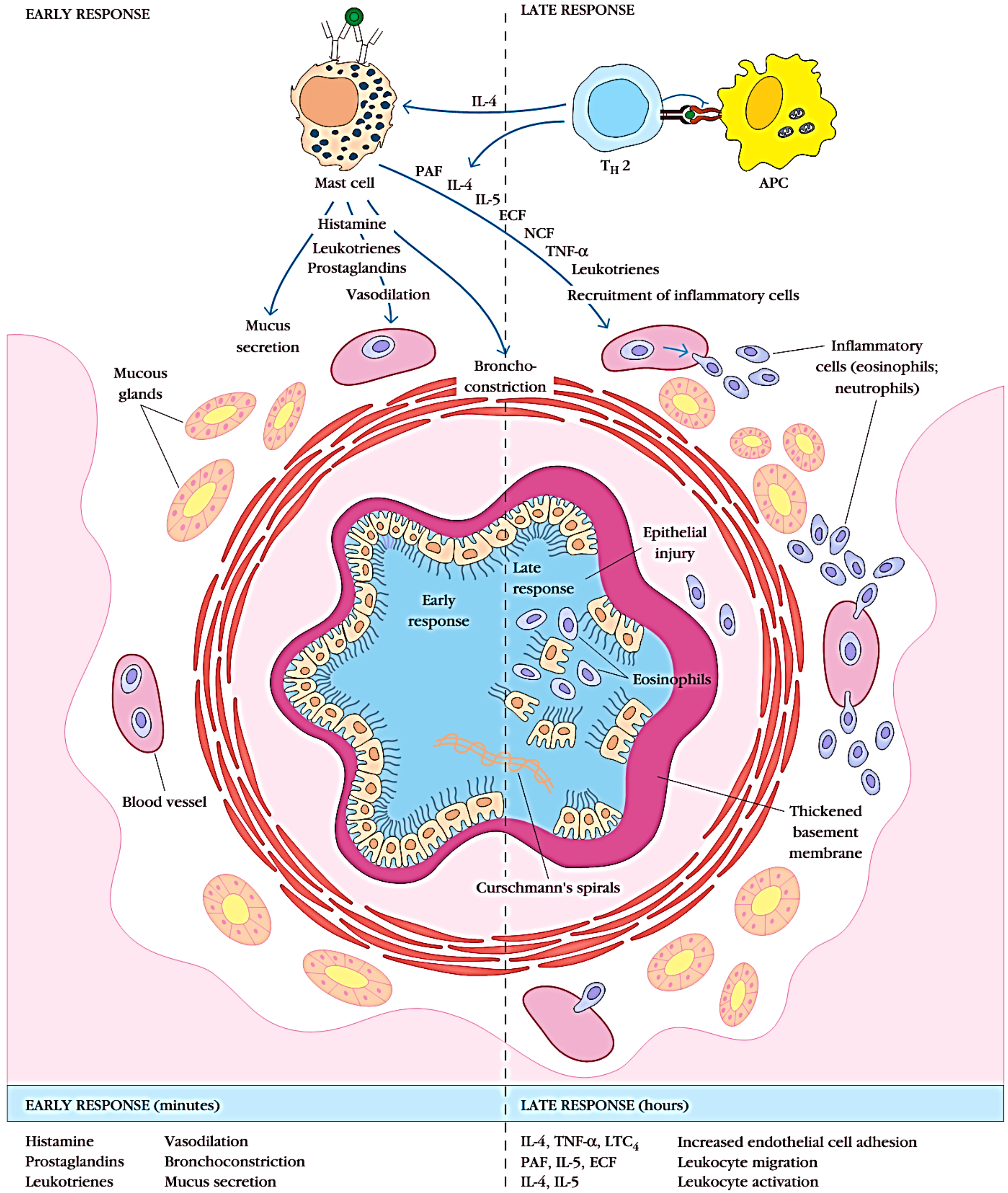


FIGURE 15-6 The early and late inflammatory responses in asthma. The immune cells involved in the early and late responses are represented at the top. The effects of various mediators on an airway, represented in cross-section, are illustrated in the center and also described in the text.

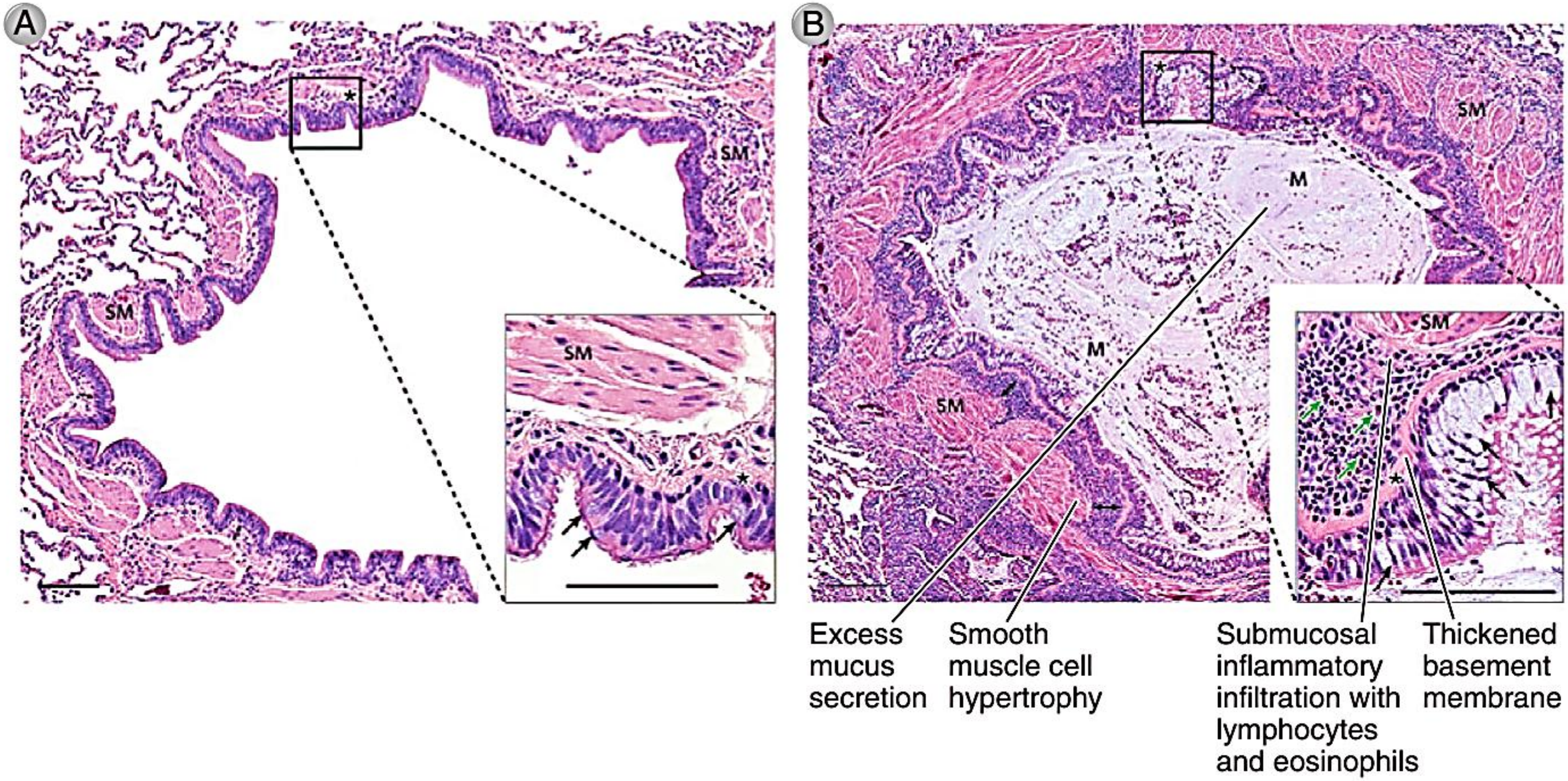
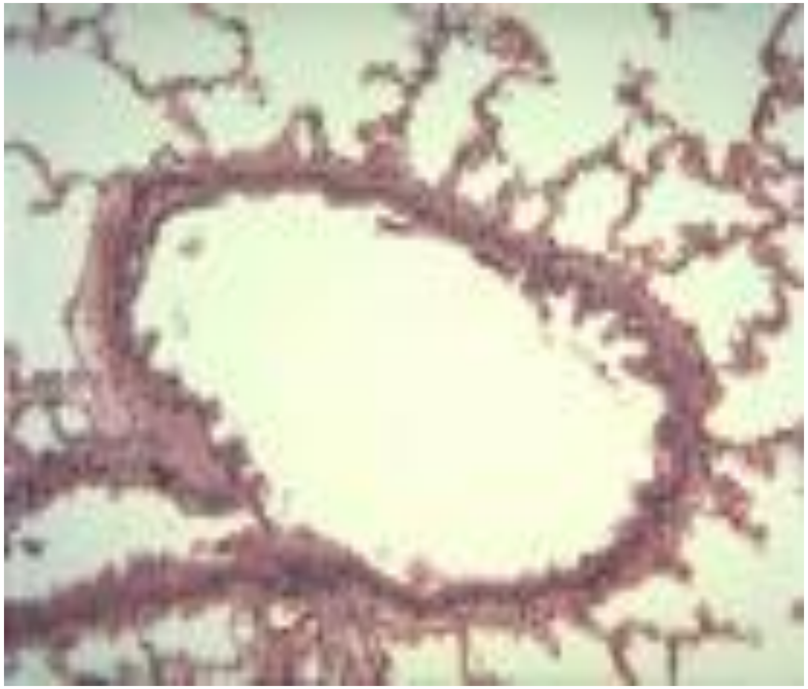
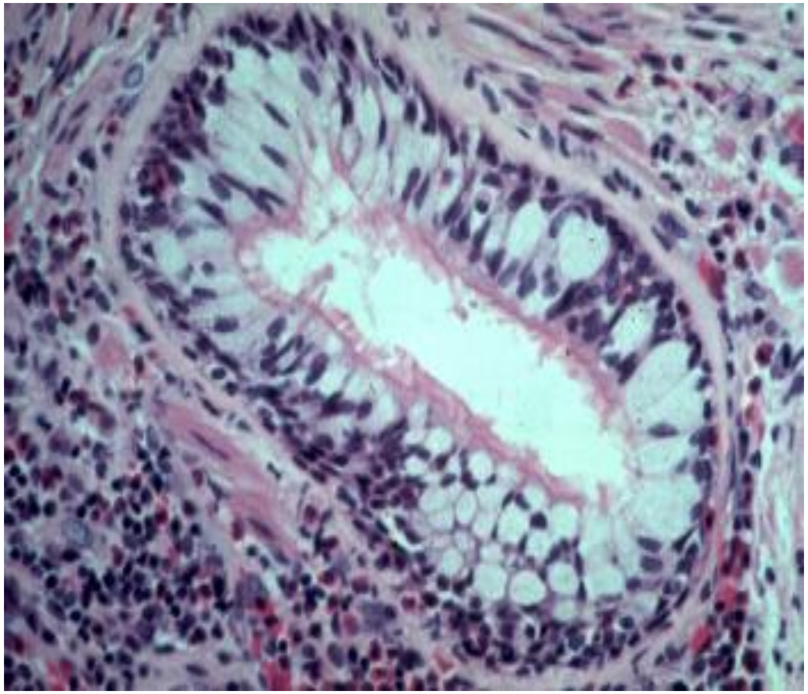


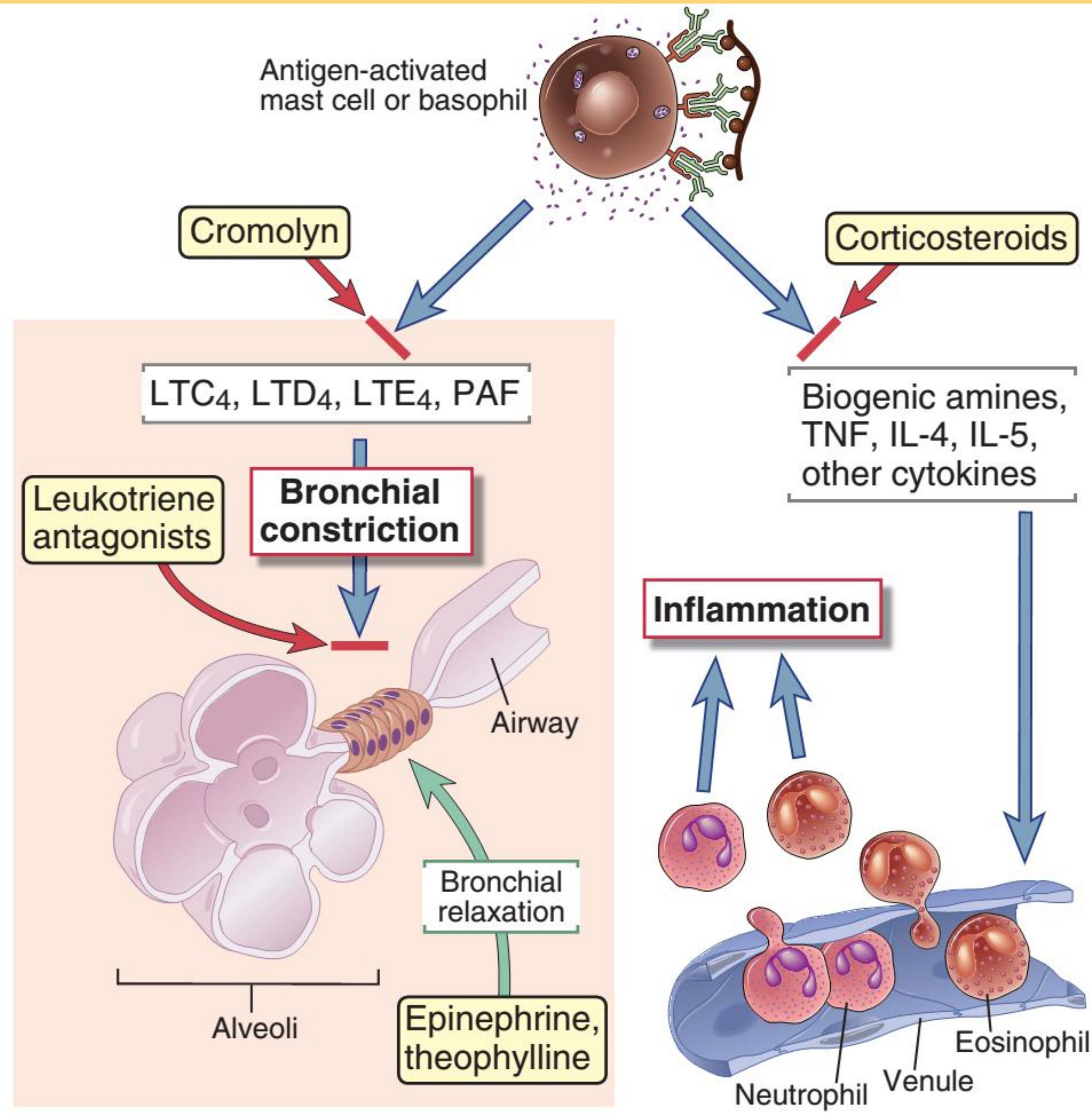
FIGURE 19–9 Histopathologic features of bronchial asthma. Atopic bronchial asthma results from repeated immediate hypersensitivity reactions in the lungs with chronic late-phase reactions. A cross-section of a normal bronchus is shown in **A;** a bronchus from a patient with asthma is shown in **B.** The diseased bronchus has excessive mucus (M) production, many submucosal inflammatory cells (including eosinophils), and smooth muscle (SM) hypertrophy, and many more goblet cells than in the normal bronchus (black arrows in insets). *(From Galli SJ, M Tsai, and AM Piliponsky. The development of allergic inflammation. Nature 454:445-454, 2008. Courtesy of G. J. Berry, Stanford University, California.)*

normal and asthmatic lung





اجزای دخیل در وقوع جریانات التهابی منجر به آسم



بازوفیل‌ها یا ماست‌سل‌های مقیم در بافت تنفسی در مواجهه با آلرژن (آنتی‌ژن حساسیت‌زا)، از دو مسیر تولید سایتوکاین و آمین‌های بیوژنیک موجب مهاجرت و ورود سلولهای التهابی به درون بافت تنفسی شده و از طرف دیگر با تولید لکوترین‌ها انقباض عضلات صاف جداره برونشیولی را سبب می‌شوند. اینگونه شرایط پاتولوژیک آسم فراهم می‌گردد. در این تصویر عملکرد مختلف انواع داروهای تخفیف‌دهنده علائم آسم در مراحل چندی از این وقایع مشخص می‌شود.

FIGURE 19–10 Mediators and treatment of asthma. Mast cell–derived leukotrienes and PAF are thought to be the major mediators of acute bronchoconstriction. Therapy is targeted both at reducing mast cell activation with inhibitors such as cromolyn and at countering mediator actions on bronchial smooth muscle by bronchodilators such as epinephrine and theophylline. These drugs also inhibit mast cell activation. Mast cell–derived cytokines are thought to be the major mediators of sustained airway inflammation, which is an example of a late-phase reaction, and corticosteroid therapy is used to inhibit cytokine synthesis. Cytokines are also produced by T_H2 cells (not shown).

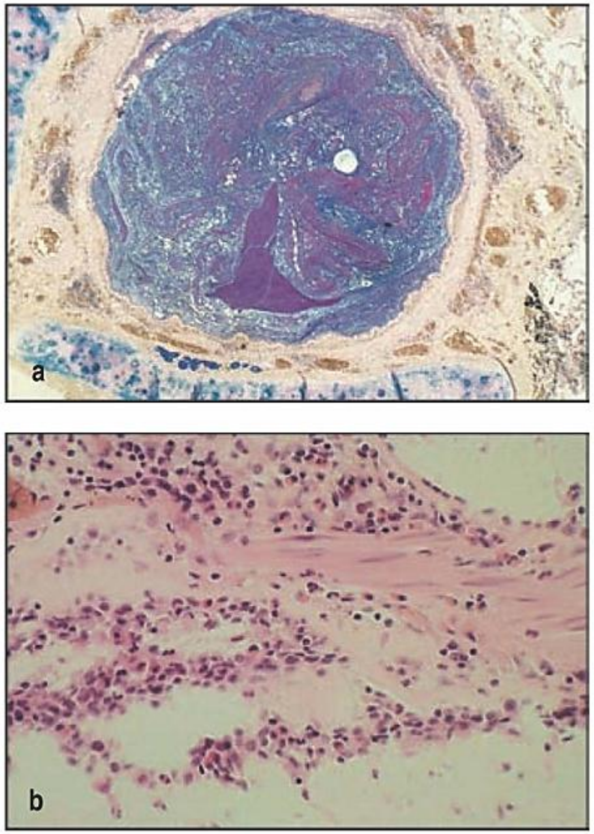


Fig. 14.16 Morphological evidence of chronic inflammation in the airways of an asthmatic patient. Panel a shows a section through a bronchus of a patient who died of asthma; there is almost total occlusion of the airway by a mucus plug. In panel b, a close-up view of the bronchial wall shows injury to the epithelium lining the bronchus, accompanied by a dense inflammatory infiltrate that includes eosinophils, neutrophils, and lymphocytes. Photographs courtesy of T. Krausz.

Probiotics and Lung Diseases

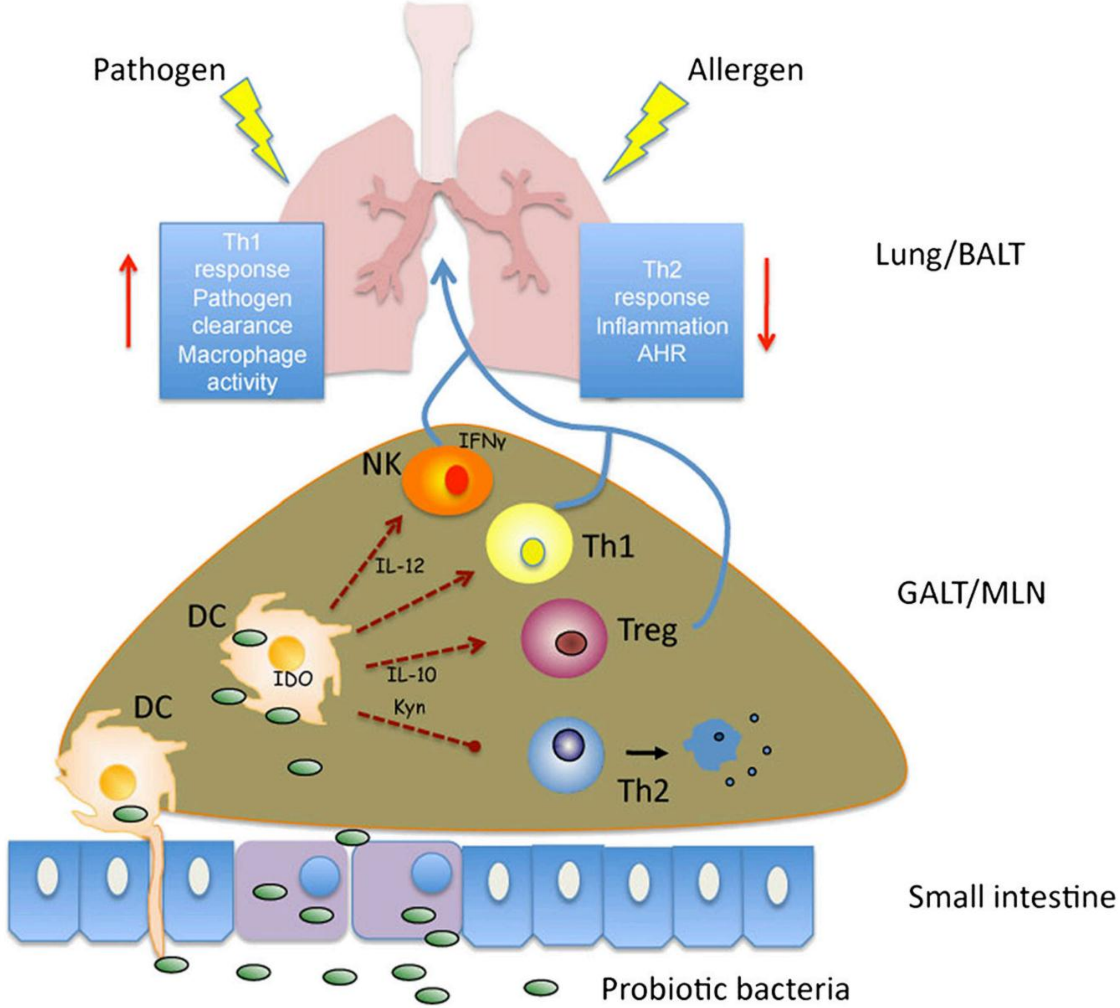


FIGURE 1. Proposed gut-lung axis of probiotic action. Microbes in the intestine are sampled by DCs either directly from the lumen or following translocation through M cells to the GALT. A combination of signals from the microbes results in phenotypic changes in the DCs and the production of Th1 type and/or regulatory mediators. IL-12 promotes Th1 cells and activation and IFN-γ production by NK cells. Regulatory cytokines such as IL-10, TGF-β, and the activation of IDO and subsequent production of immunoactive KYNs promotes Tregs and depletes Th2 cells. Following immune challenge in the airway, cells activated in the GALT and MLN traffic to the respiratory mucosa where they promote protective and antiinflammatory responses. AHR = airway hyperresponsiveness; BALT = bronchus-associated lymphoid tissue; DC = dendritic cell; GALT = gut-associated lymphoid tissue; IDO = indolamine 2,3 dioxygenase; IFN = interferon; Kyn = kynurenine; MLN = mesenteric lymph node; NK = natural killer; TGF = transforming growth factor; Th = T helper; Treg = regulatory T cell.

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overview of immune defects caused by smoking in the lungs.

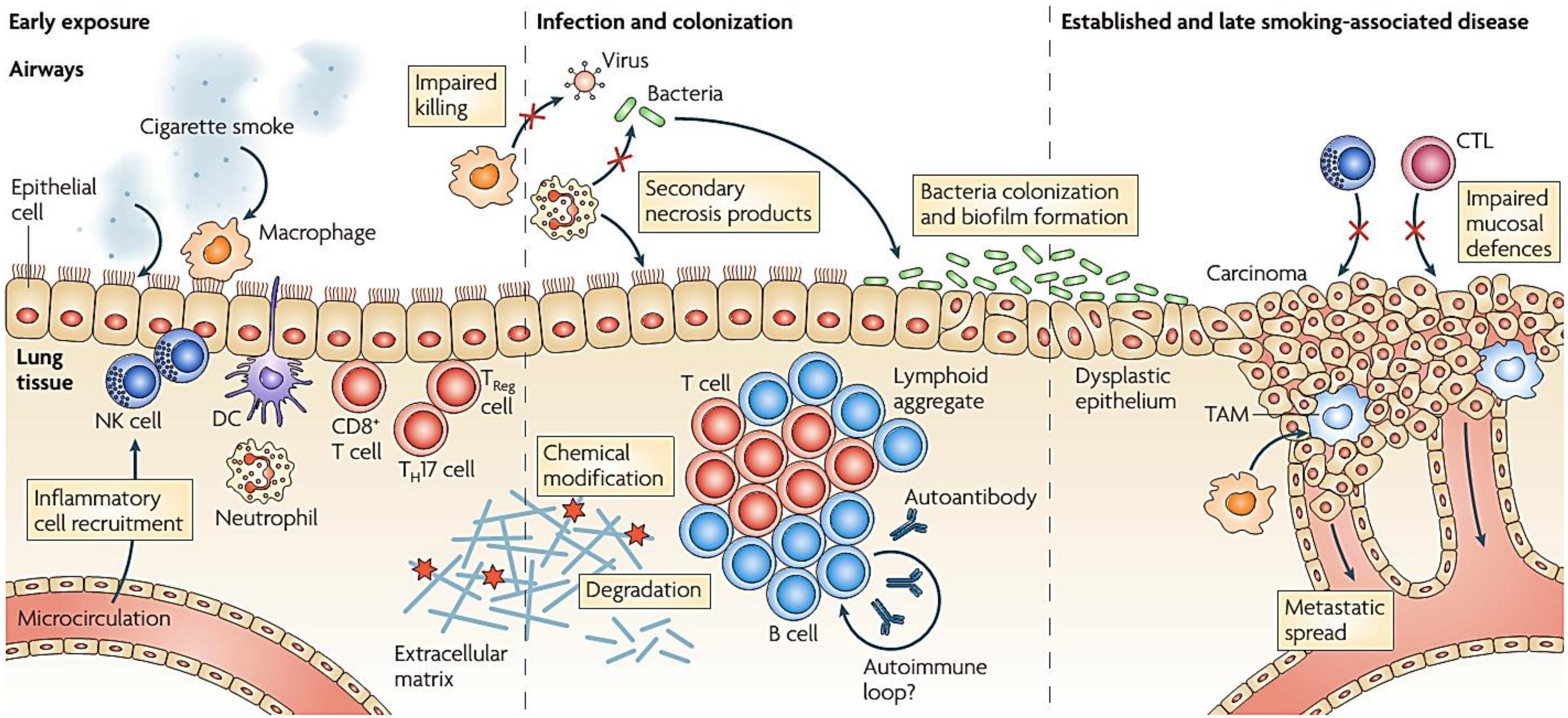


Figure 2 | **Overview of immune defects caused by smoking in the lungs.** Cigarette smoke has both pro-inflammatory and immunosuppressive effects on the immune system. Acute effects of smoke on macrophages and epithelial cells promote inflammation by inducing the recruitment of cells from the microcirculation to the lungs. At the same time, cigarette smoke impairs innate defence mechanisms that are mediated by macrophages, epithelial cells, dendritic cells (DCs) and natural killer (NK) cells, thereby increasing the risk, severity and duration of infection. The transition to a more severe expression of smoking-associated disease is marked by the impaired ability of macrophages to kill bacteria or viruses, the loss of the ability to remove dead cells, the degradation and chemical modification of the extracellular matrix, the increasing retention of oligoclonally expanded $CD8^+$ T cells and the induction of interleukin-17 (IL-17)-secreting effector T cells. After long-term exposure to cigarette smoke, lymphoid aggregates with T cells and B cell zones may form at the site, supporting the production of pathogenic autoantibodies and driving autoimmune disease. Loss of mucosal defences can lead to bacterial colonization (as occurs in around 30% of long-term smokers with chronic obstructive pulmonary disease (COPD)). Concurrently somatic mutations in the epithelium and alteration of macrophage phenotype promote inflammation and the development of cancer (carcinoma *in situ*) that has a high chance of metastatic spread. CTL, cytotoxic T lymphocyte; TAM, tumour-associated macrophage; T_H17, T helper 17; T_{Reg}, regulatory T.

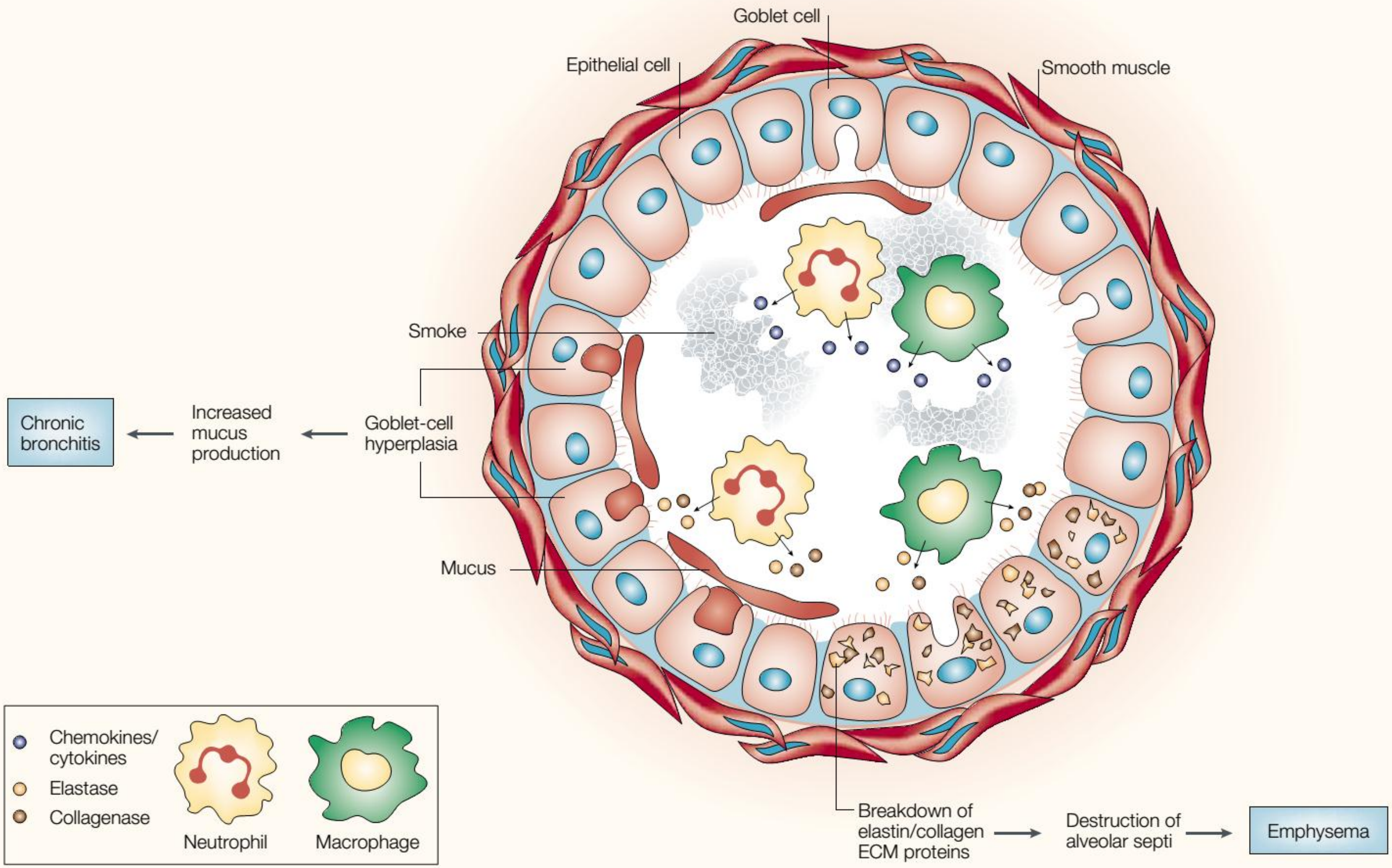


Figure 2 | **Simplified schematic of the mechanism by which cigarette smoke might cause COPD.** Neutrophils and macrophages accumulate in the lungs of smokers, leading to inflammation and the release of cellular products, such as enzymes that break down collagen and elastin in the lung and/or stimulate mucus production, resulting in emphysema and/or chronic bronchitis, respectively. COPD, chronic obstructive pulmonary disease; ECM, extracellular matrix.

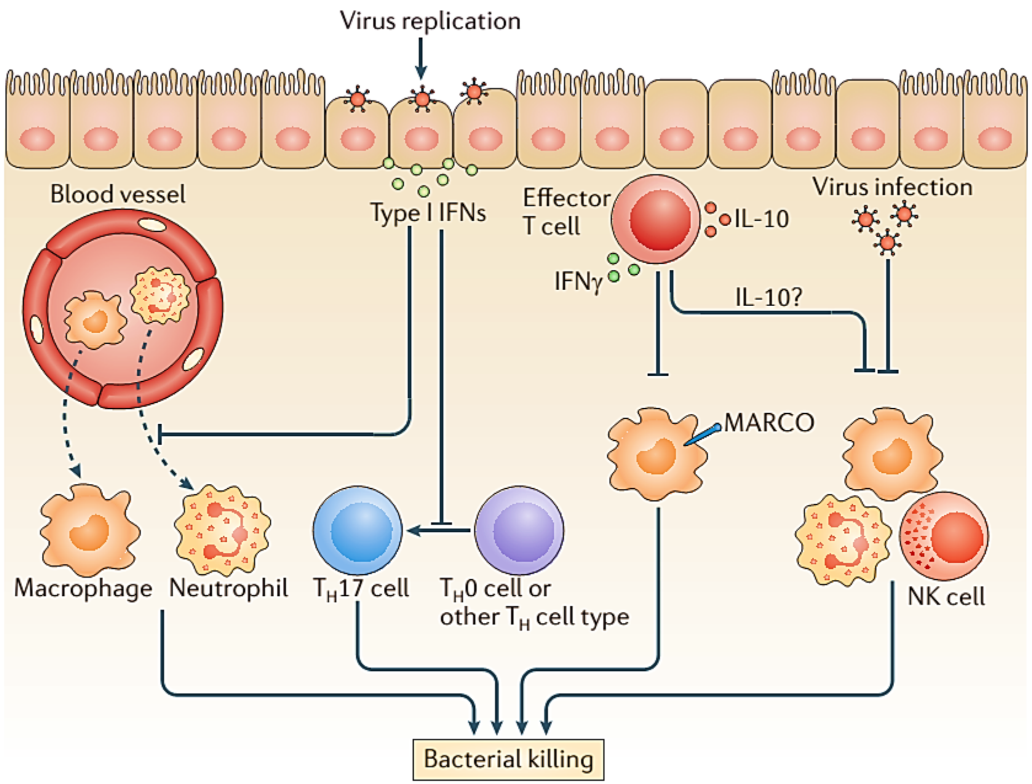
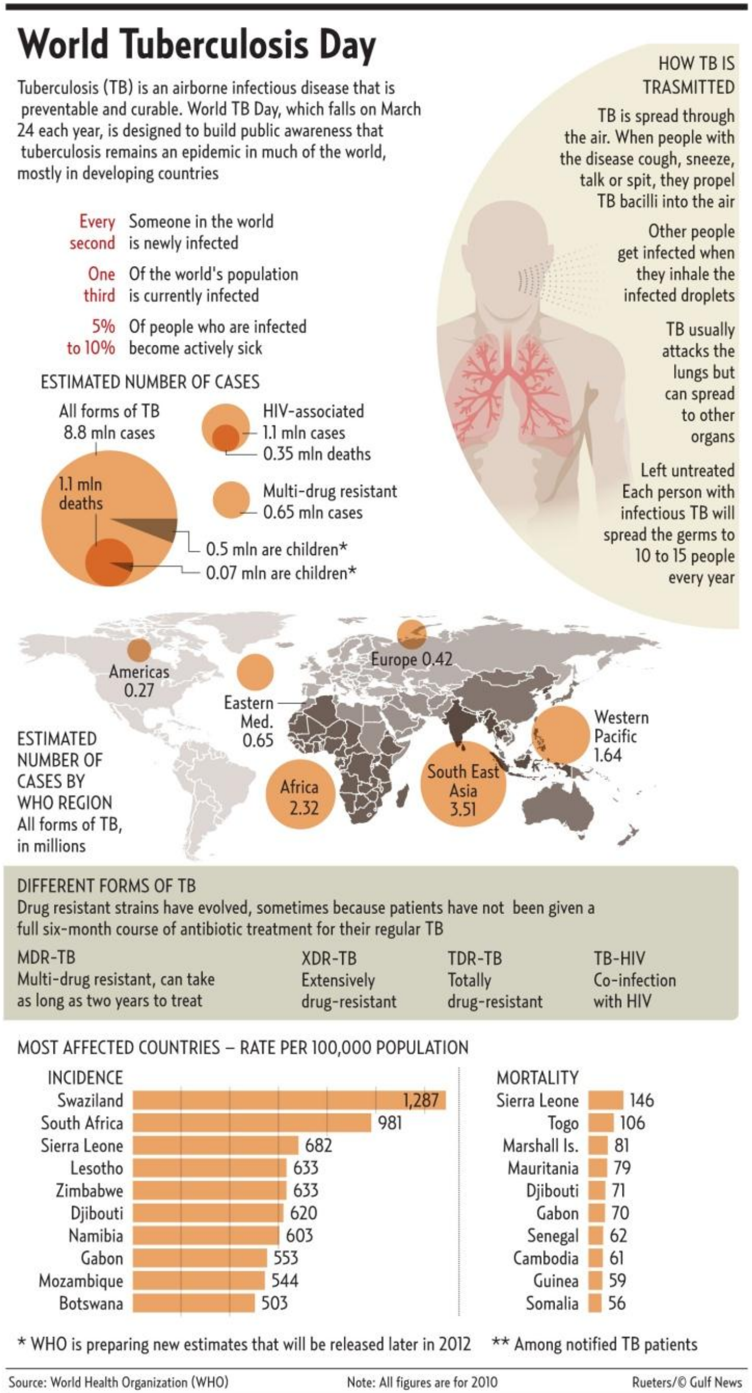
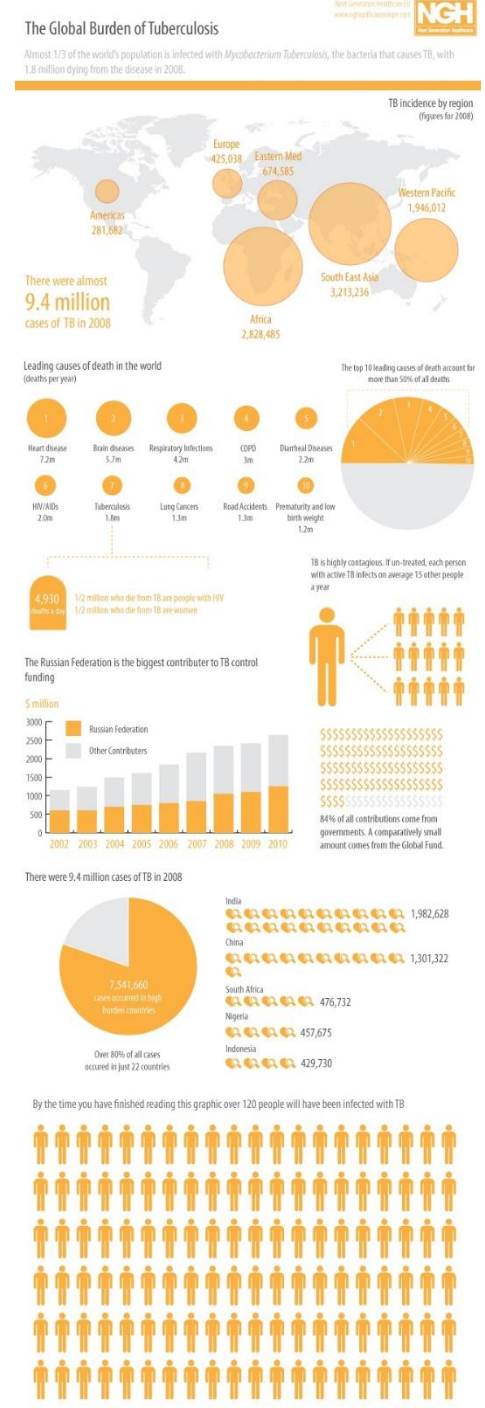
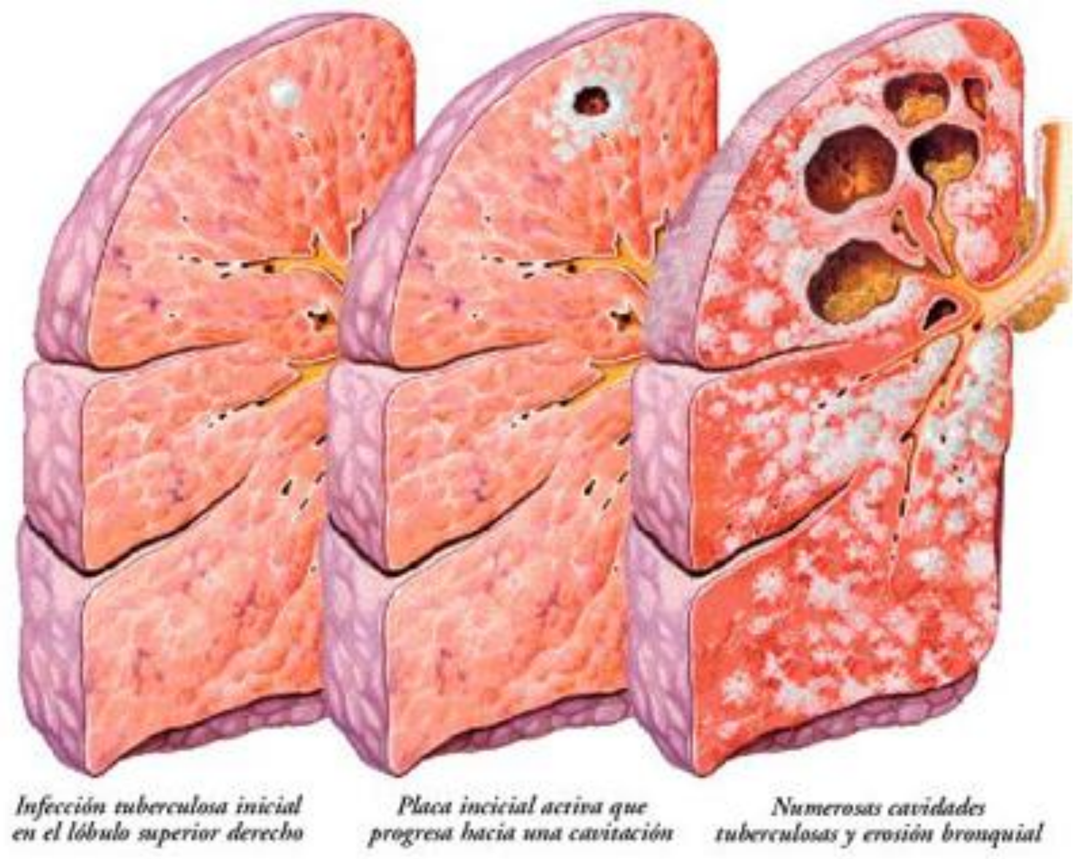


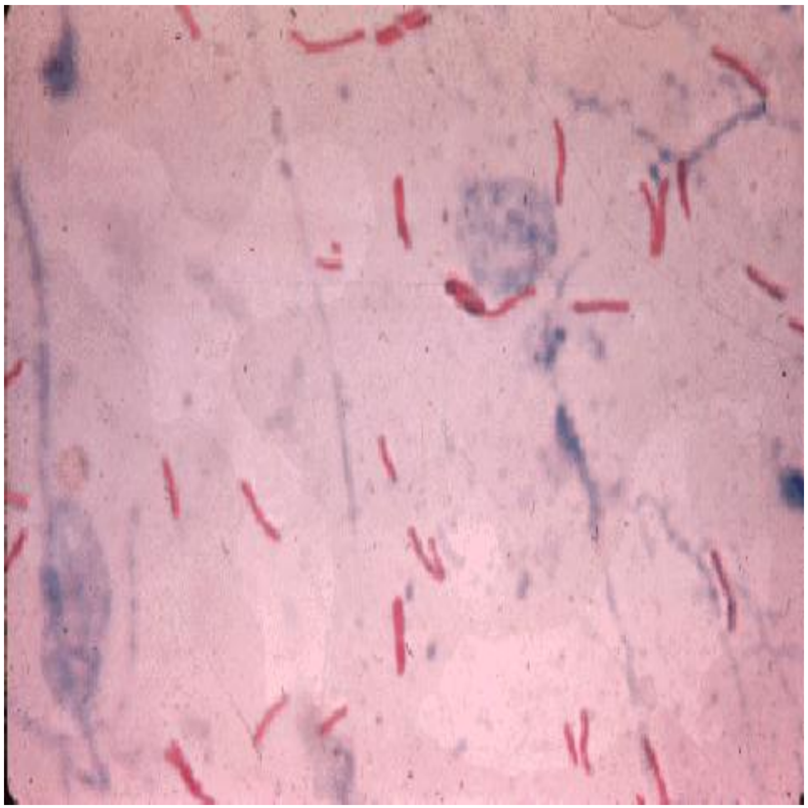
Figure 3 | **Respiratory virus infection and susceptibility to secondary bacterial infection.** Multiple distinct mechanisms have been postulated to account for the increased susceptibility to bacterial superinfection and bacterial pneumonia following infection with respiratory viruses such as type A influenza viruses. Influenza virus infection induces the production of type I interferons (IFNs), which inhibit the recruitment of circulating neutrophils and macrophages to the lung following bacterial challenge. Type I IFNs also inhibit the differentiation of antibacterial T helper 17 (T_H17) cells from naive T cells (T_H0 cells) or other T_H cell types (such as T_H1 and T_H2 cells)[110] and thereby potentiate host susceptibility to secondary bacterial infection. IFNγ production by influenza virus-specific effector T cells decreases the expression of macrophage receptor with collagenous structure (MARCO) by alveolar macrophages and inhibits the ingestion of bacteria by these cells. Moreover, interleukin-10 (IL-10) production by influenza virus-specific effector T cells may inhibit the ability of innate immune cells, in particular macrophages, to kill bacteria. Finally, the direct interaction and/or infection of innate immune cells — such as macrophages, neutrophils and natural killer (NK) cells — with influenza virus suppresses the ability of these cells to take up and kill bacteria.

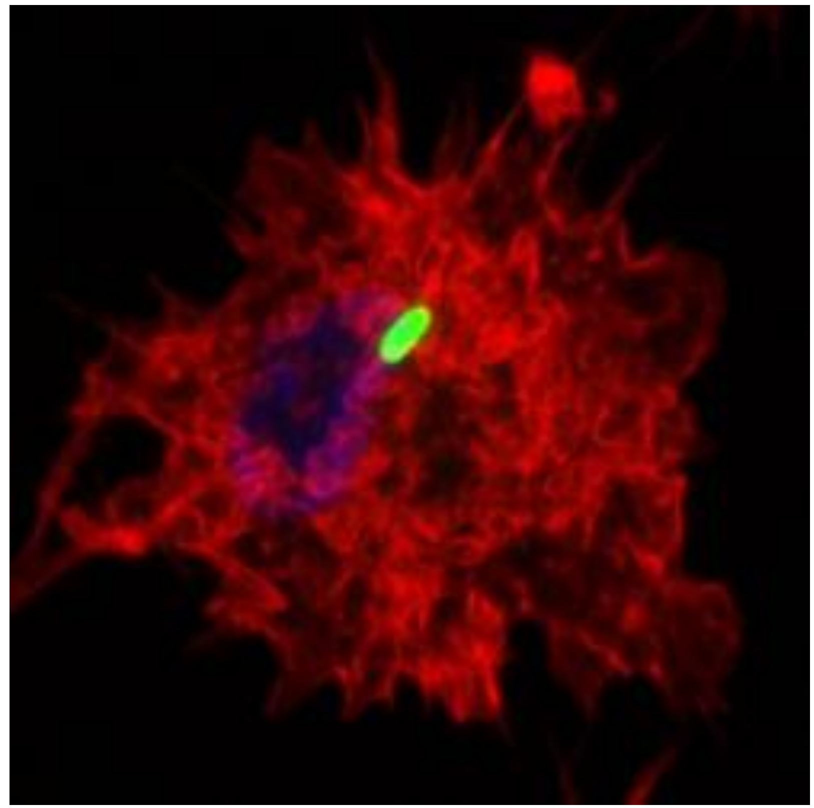

World Tuberculosis Day
Tuberculosis (TB) is an airborne infectious disease that is preventable and curable. World TB Day, which falls on March 24 each year, is designed to build public awareness that tuberculosis remains an epidemic in much of the world, mostly in developing countries
Every second Someone in the world is newly infected
One third Of the world's population is currently infected
5% to 10% Of people who are infected become actively sick
ESTIMATED NUMBER OF CASES
All forms of TB 8.8 mln cases
1.1 mln deaths
0.5 mln are children*
0.07 mln are children*
HIV-associated
1.1 mln cases
0.35 mln deaths
Multi-drug resistant 0.65 mln cases
HOW TB IS TRASMITTED
TB is spread through the air. When people with the disease cough, sneeze, talk or spit, they propel TB bacilli into the air
Other people get infected when they inhale the infected droplets
TB usually attacks the lungs but can spread to other organs
Left untreated Each person with infectious TB will spread the germs to 10 to 15 people every year
Americas 0.27
Eastern Med. 0.65
Europe 0.42
Africa 2.32
South East Asia 3.51
Western Pacific 1.64
ESTIMATED NUMBER OF CASES BY WHO REGION All forms of TB, in millions
DIFFERENT FORMS OF TB
Drug resistant strains have evolved, sometimes because patients have not been given a full six-month course of antibiotic treatment for their regular TB
MDR-TB Multi-drug resistant, can take as long as two years to treat
XDR-TB Extensively drug-resistant
TDR-TB Totally drug-resistant
TB-HIV Co-infection with HIV
MOST AFFECTED COUNTRIES – RATE PER 100,000 POPULATION
INCIDENCE
Swaziland 1,287
South Africa 981
Sierra Leone 682
Lesotho 633
Zimbabwe 633
Djibouti 620
Namibia 603
Gabon 553
Mozambique 544
Botswana 503
MORTALITY
Sierra Leone 146
Togo 106
Marshall Is. 81
Mauritania 79
Djibouti 71
Gabon 70
Senegal 62
Cambodia 61
Guinea 59
Somalia 56
* WHO is preparing new estimates that will be released later in 2012
** Among notified TB patients
Source: World Health Organization (WHO)
Note: All figures are for 2010
Rueters/© Gulf News


The Global Burden of Tuberculosis
NGH
Almost 1/3 of the world's population is infected with Mycobacterium Tuberculosis, the bacteria that causes TB, with 1.8 million dying from the disease in 2008.
TB incidence by region (figures for 2008)
Europe 425,038
Eastern Med 674,585
Americas 281,682
Western Pacific 1,946,012
South East Asia 3,213,236
Africa 2,828,485
There were almost 9.4 million cases of TB in 2008
Leading causes of death in the world (deaths per year)
Heart disease 7.2m
Brain diseases 5.7m
Respiratory Infections 4.2m
COPD 3m
Diarrheal Diseases 2.2m
HIV/AIDs 2.0m
Tuberculosis 1.8m
Lung Cancers 1.3m
Road Accidents 1.3m
Prematurity and low birth weight 1.2m
The top 10 leading causes of death account for more than 50% of all deaths
4,930 deaths a day
1/2 million who die from TB are people with HIV
1/2 million who die from TB are women
TB is highly contagious. If un-treated, each person with active TB infects on average 15 other people a year
The Russian Federation is the biggest contributer to TB control funding
$ million
Russian Federation
Other Contributers
3000
2500
2000
1500
1000
500
0
2002 2003 2004 2005 2006 2007 2008 2009 2010
84% of all contributions come from governments. A comparatively small amount comes from the Global Fund.
There were 9.4 million cases of TB in 2008
7,541,660 cases occurred in high burden countries
Over 80% of all cases occured in just 22 countries
India 1,982,628
China 1,301,322
South Africa 476,732
Nigeria 457,675
Indonesia 429,730
By the time you have finished reading this graphic over 120 people will have been infected with TB
Source: World Health Organisation


Infección tuberculosa inicial
en el lóbulo superior derecho
Placa inicicial activa que
progresa hacia una cavitación
Numerosas cavidades
tuberculosas y erosión bronquial

M. tuberculosis inside macrophage





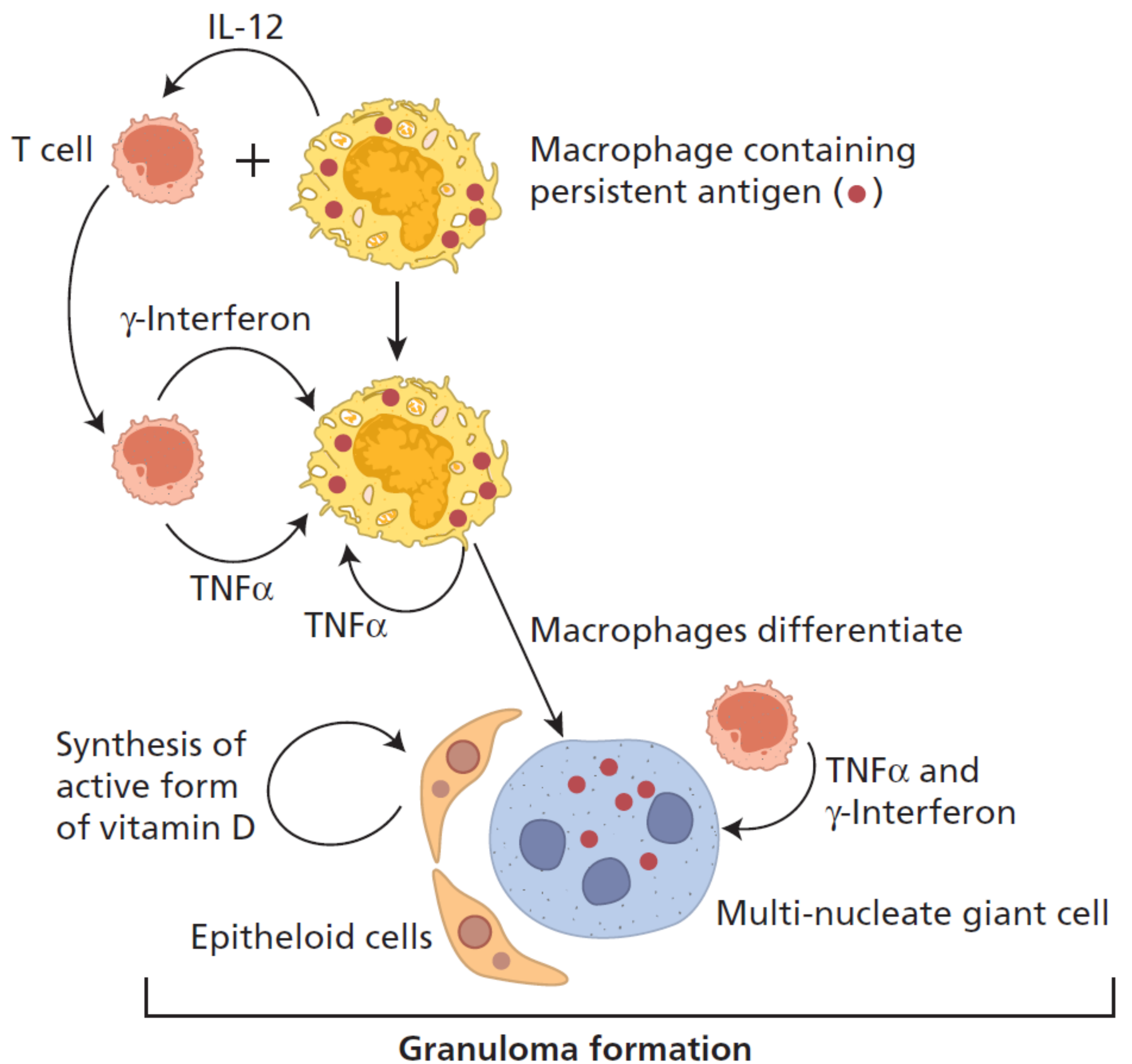


Fig. 13.4 Mechanisms of T-cell-dependent granuloma formation.

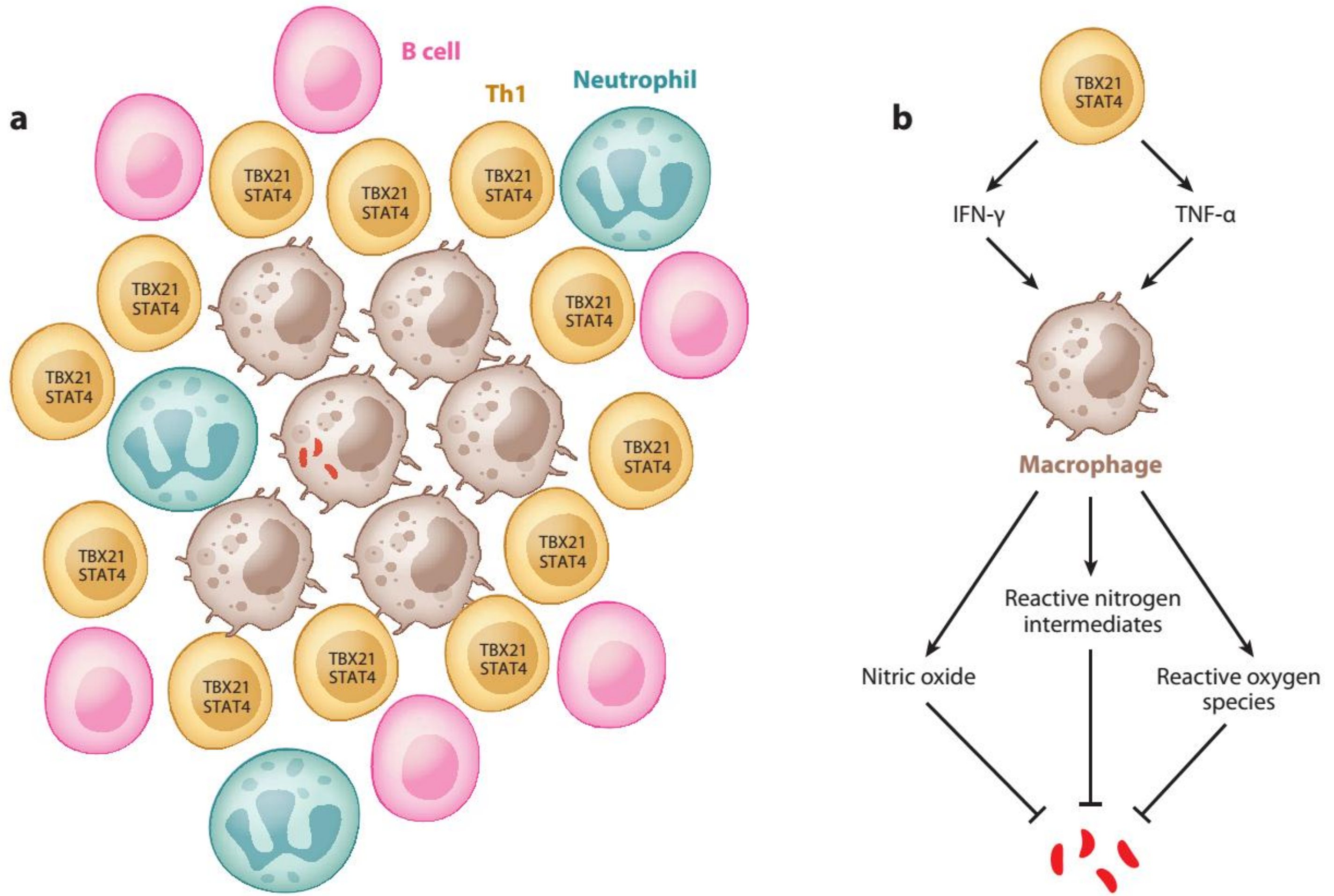
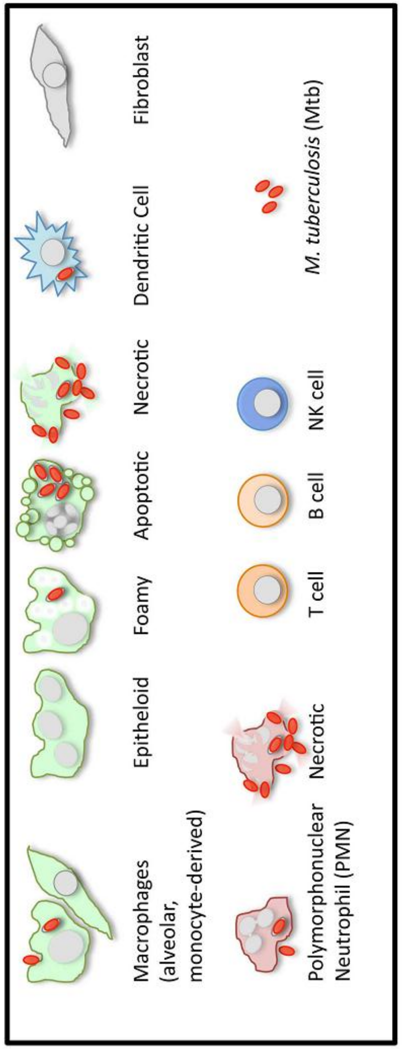


Figure 2

Th1 cells and granuloma formation. (*a*) Schematic representation of granuloma structure: An infected macrophage is surrounded by many cell types such as uninfected macrophages, Th1 cells, B cells, and neutrophils. (*b*) Functions of Th1 cells in tuberculosis: Th1 cells activate macrophages via cytokines such as TNF-α and IFN-γ. Activated macrophages kill bacteria through nitric oxide, reactive nitrogen intermediates, and reactive oxygen species (see text for details).



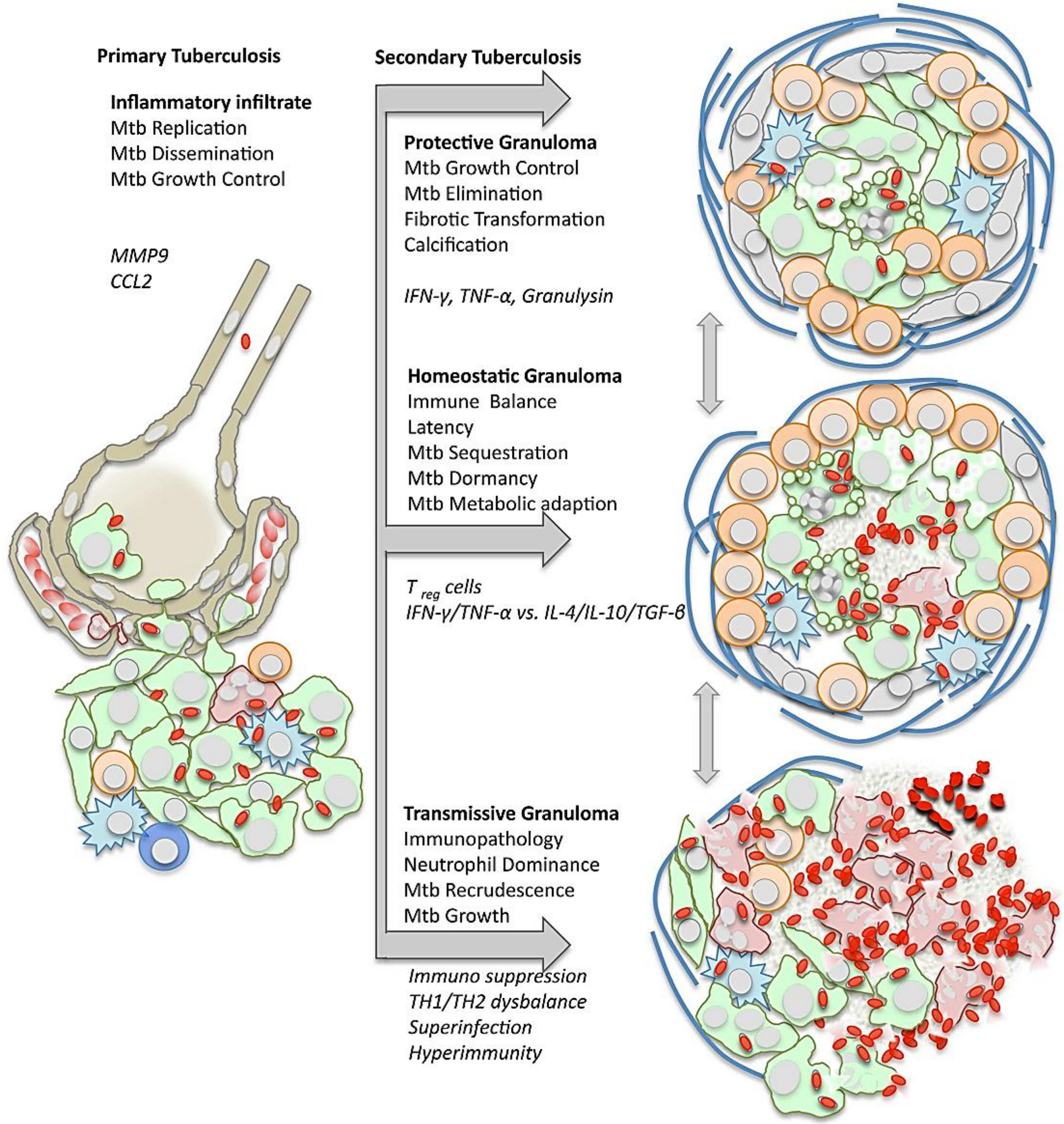
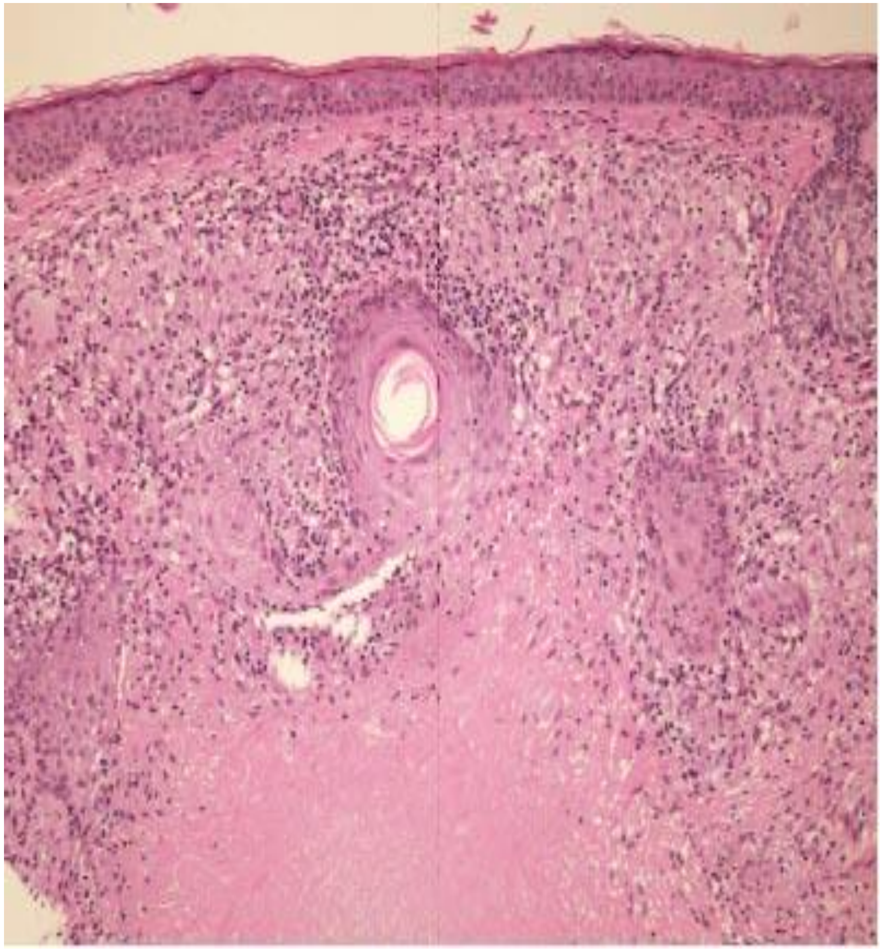
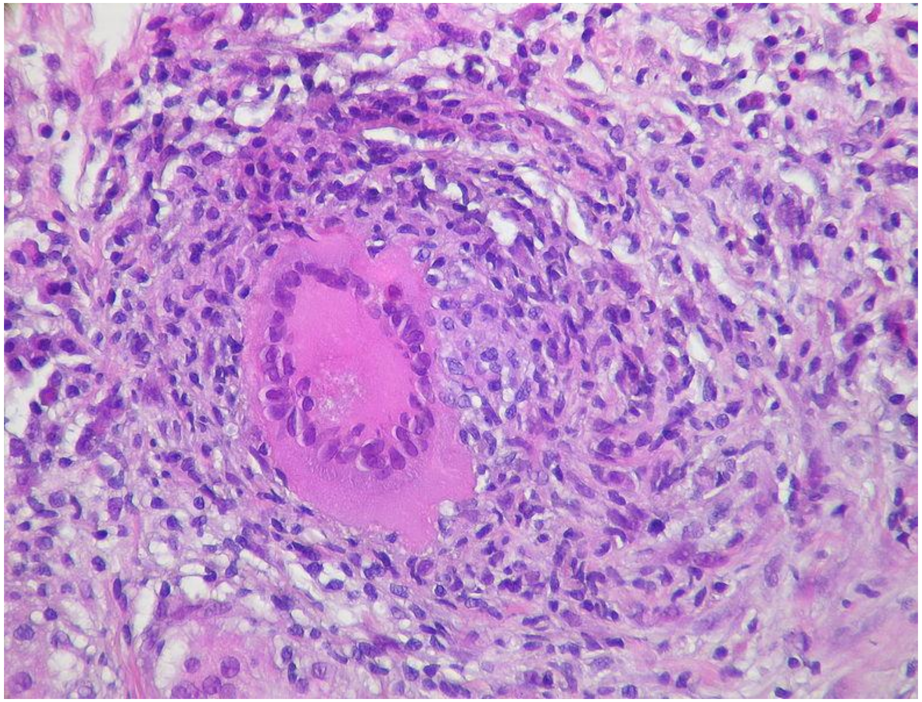


FIGURE 1 | Dynamics of granuloma formation and pathology in tuberculosis. *M. tuberculosis* (Mtb) elicits a local inflammatory infiltrate which may give rise to (i) protective immunity, (ii) balanced inflammation (i.e., control of Mtb growth with little tissue damage), or (iii) endobronchial transmission following granuloma necrosis. The depicted types of organized granulomas are idealized and represent stages of a pathophysiological continuum. At the same time, they represent stages of the Mtb life cycle with either retarded growth or metabolic adaptation within the granulomatous lesion, or recrudescence and spreading to the next host following granuloma disruption. Italics indicate typical cellular and humoral mediators involved in granuloma differentiation which are addressed in more detail in the text.





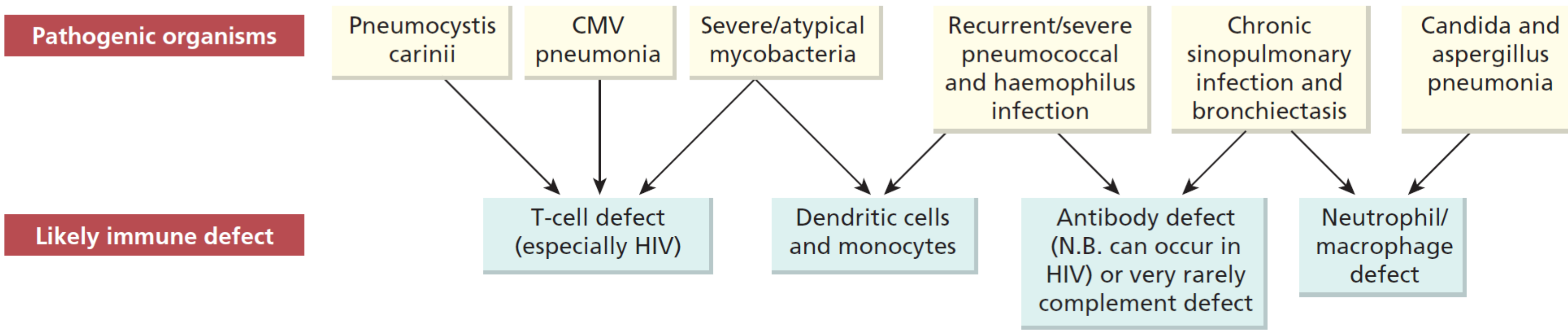
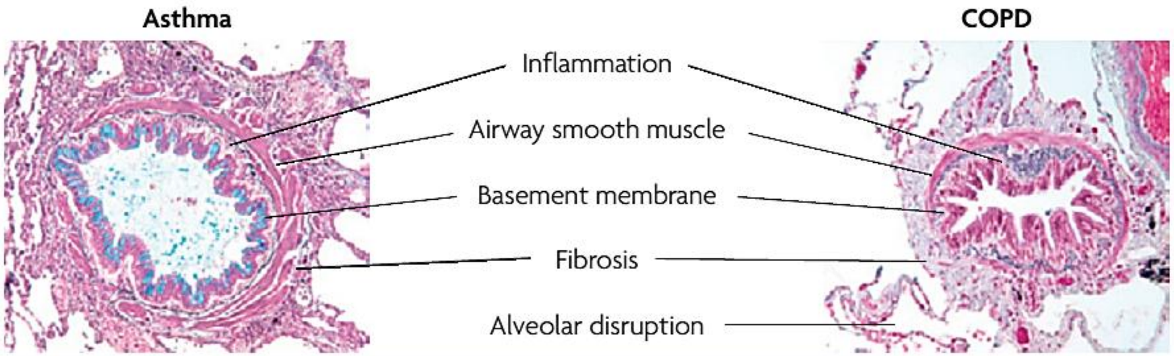


Fig. 13.2 Patterns of respiratory infection associated with specific immunodeficiencies. CMV, Cytomegalovirus; HIV, human immunodeficiency virus.



	Asthma	COPD
Inflammation	+++	+++
Airway smooth muscle	+++	+
Basement membrane	++	–
Fibrosis	+ (subepithelial)	+++ (peribronchiolar)
Alveolar disruption	–	+++
Airway vessels	++	No change
Mast cells	++ (and activated)	Normal
Dendritic cells	++	ND
Eosinophils	++	Normal
Neutrophils	Normal	++
Lymphocytes	T_H2 type	T_H1 and T_C1 type
Epithelium	Often shed	Pseudostratified
Goblet cells	++	++

Figure 3 | **Contrasting histopathology of asthma and chronic obstructive pulmonary disease (COPD).** A small airway from a patient who died from asthma and a similar sized airway from a patient with severe COPD are shown. There is an infiltration of inflammatory cells in both diseases. The airway smooth-muscle cell layer is thickened in asthma but only to a minimal degree in COPD. The basement membrane is thickened in asthma due to collagen deposition (subepithelial fibrosis) but not in COPD, whereas in COPD collagen is deposited mainly around the airway (peribronchiolar fibrosis). The alveolar attachments are intact in asthma, but disrupted in COPD as a result of emphysema. Images courtesy of Dr J. Hogg (Vancouver, Canada). Other differences in the cellular infiltrate in the two diseases are also shown. ND, not determined; T_C1, type 1 cytotoxic T; T_H1, T helper 1.

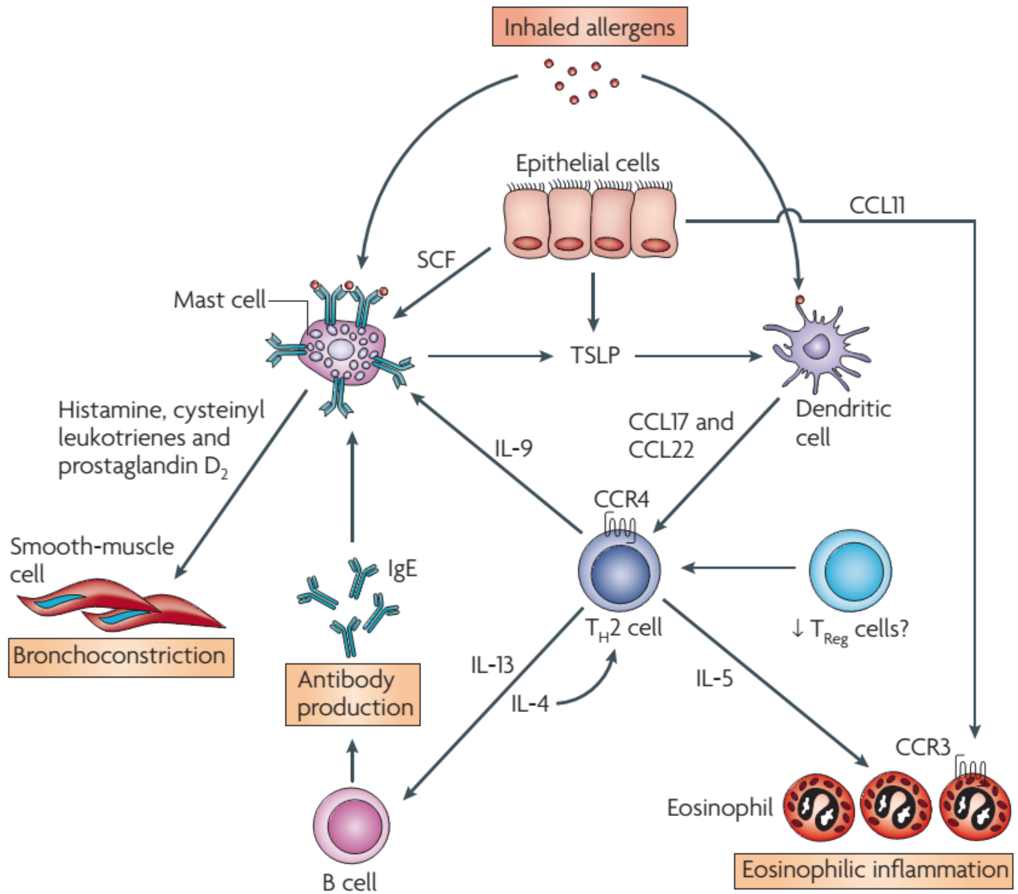


Figure 1 | **Inflammatory and immune cells involved in asthma.** Inhaled allergens activate sensitized mast cells by crosslinking surface-bound IgE molecules to release several bronchoconstrictor mediators, including cysteinyl leukotrienes and prostaglandin D_2. Epithelial cells release stem-cell factor (SCF), which is important for maintaining mucosal mast cells at the airway surface. Allergens are processed by myeloid dendritic cells, which are conditioned by thymic stromal lymphopoietin (TSLP) secreted by epithelial cells and mast cells to release the chemokines CC-chemokine ligand 17 (CCL17) and CCL22, which act on CC-chemokine receptor 4 (CCR4) to attract T helper 2 (T_H2) cells. T_H2 cells have a central role in orchestrating the inflammatory response in allergy through the release of interleukin-4 (IL-4) and IL-13 (which stimulate B cells to synthesize IgE), IL-5 (which is necessary for eosinophilic inflammation) and IL-9 (which stimulates mast-cell proliferation). Epithelial cells release CCL11, which recruits eosinophils via CCR3. Patients with asthma may have a defect in regulatory T (T_{Reg}) cells, which may favour further T_H2-cell proliferation.

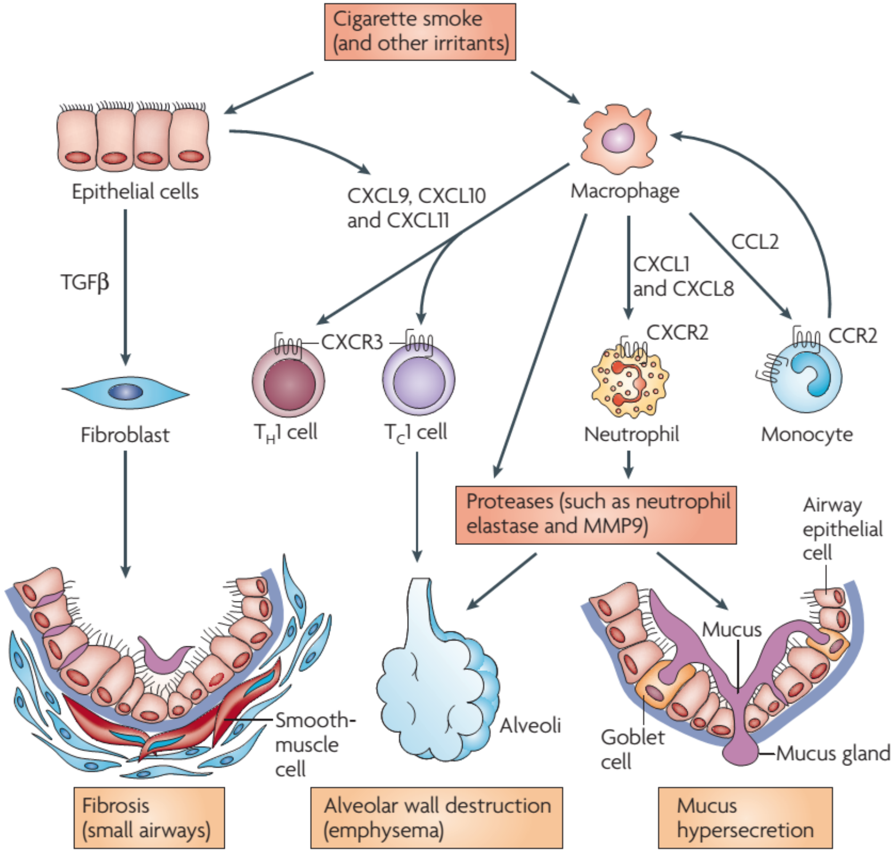


Figure 2 | **Inflammatory and immune cells involved in chronic obstructive pulmonary disease (COPD).** Inhaled cigarette smoke and other irritants activate epithelial cells and macrophages to release several chemotactic factors that attract inflammatory cells to the lungs, including CC-chemokine ligand 2 (CCL2), which acts on CC-chemokine receptor 2 (CCR2) to attract monocytes, CXC-chemokine ligand 1 (CXCL1) and CXCL8, which act on CCR2 to attract neutrophils and monocytes (which differentiate into macrophages in the lungs) and CXCL9, CXCL10 and CXCL11, which act on CXCR3 to attract T helper 1 (T_H1) cells and type 1 cytotoxic T (T_C1) cells. These inflammatory cells together with macrophages and epithelial cells release proteases, such as matrix metalloproteinase 9 (MMP9), which cause elastin degradation and emphysema. Neutrophil elastase also causes mucus hypersecretion. Epithelial cells and macrophages also release transforming growth factor-β (TGFβ), which stimulates fibroblast proliferation, resulting in fibrosis in the small airways.

Table 13.1 Respiratory infections classified according to site and pattern of infection

Site	Organism	Incidence and pattern of infection	Predisposing factors
Upper respiratory tract	Viral	Common – colds	
	Bacterial	Less common – sinusitis	Physical damage
			Viral infection
			Immune dysfunction
Lower respiratory tract	Viral	Pneumonia – rare in adults	Immune dysfunction
		Bronchiolitis due to respiratory syncytial virus common in children	
	Bacterial	Common	Age
			Smoking
			Immune dysfunction

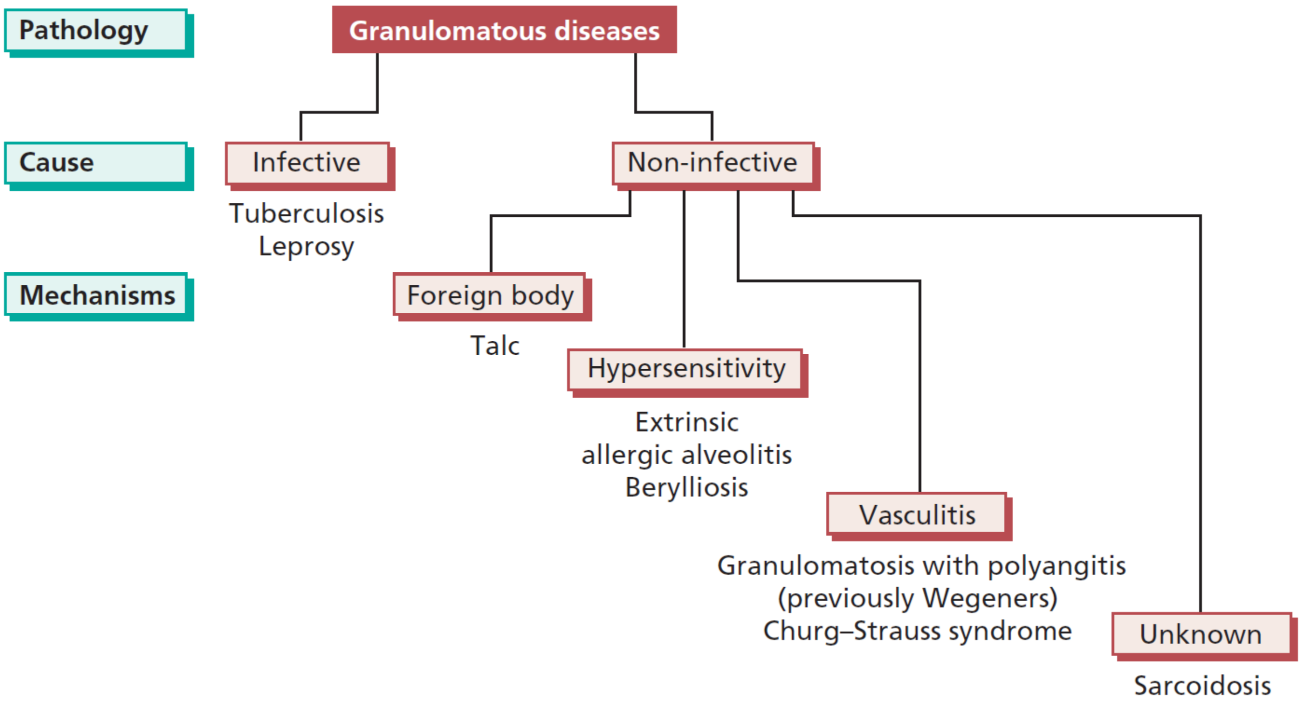


Fig. 13.3 A classification of granulomatous lung diseases.

Table 13.5 Major causes of interstitial lung disease and pulmonary fibrosis

Systemic autoimmune diseases
Inorganic dusts • Asbestos • Silica
Hypersensitivity to known inhaled antigens • Extrinsic allergic alveolitis • Berylliosis
Drug hypersensitivity/toxicity • Cytotoxic drugs (e.g. bleomycin) • Paraquat poisoning • Drugs associated with eosinophilic pneumonia (e.g. nitrofurantoin) • Methotrexate
Pulmonary eosinophilia
Granulomatous diseases • Sarcoidosis • Tuberculosis
Idiopathic interstitial pneumonias

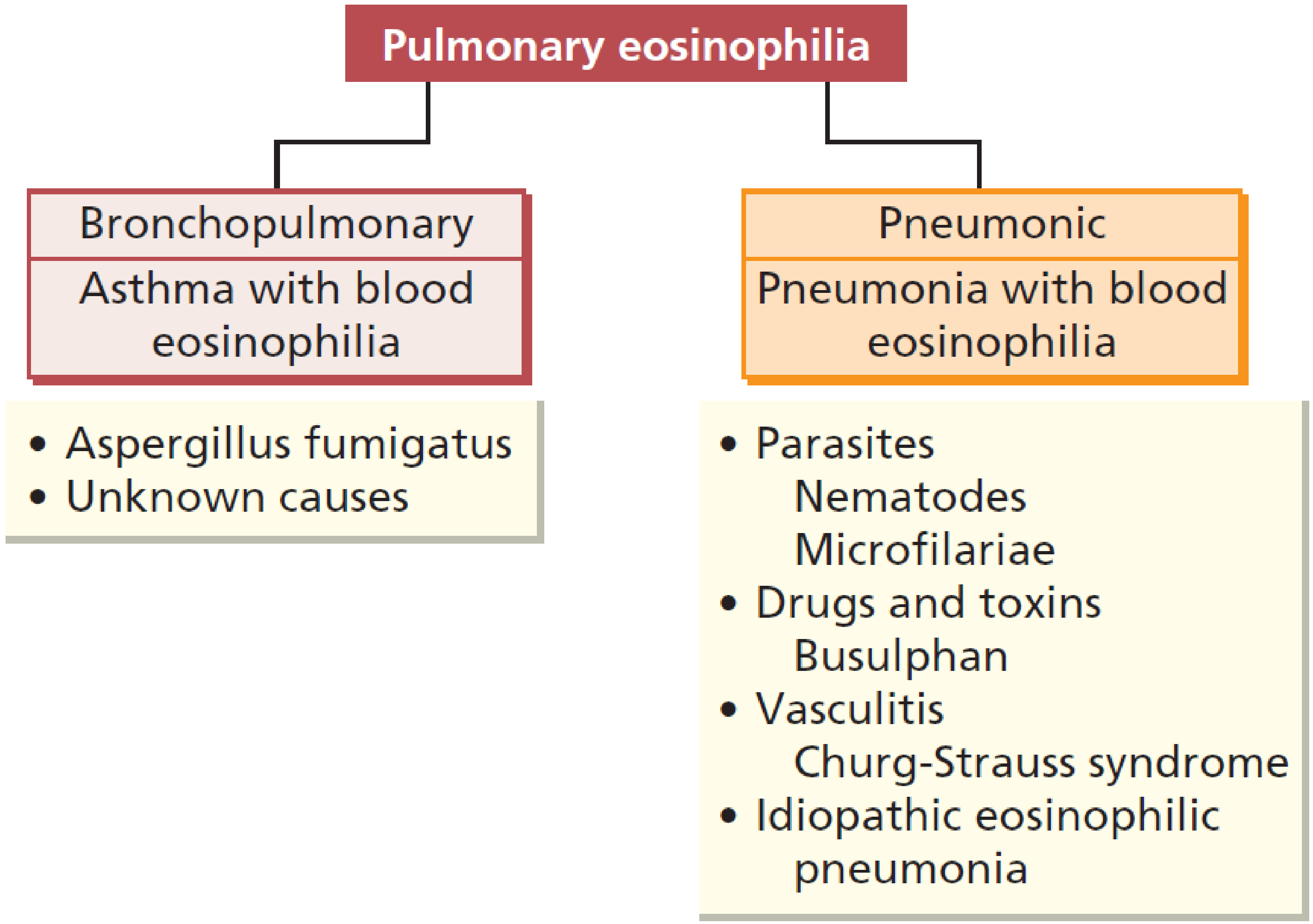


Fig. 13.7 Classification and causes of pulmonary eosinophilia.

Disease Entity	Type of the immune reaction	Major Features
Asthma	**I type**	**IgE mediated**
Drug-induced lung diseases & reactions	**Cytotoxic type II** **CMI**	**The drug is a hapten → Ab or sens. Ly**
Hypersensitive pneumonitis ABPA	**Type III immune complexes & CMI** **Type I & Type III**	**Exposure to exogenous allergen**
Lung Tuberculosis	**CMI**	
Sarcoidosis	**CMI**	**Granulomatous inflammation**
Autoimmune-Mediated Diseases	**Immune Complexes** **type III**	**Multiple pathogenesis**
Pulmonary Vasculitis Syndromes	**Autoimmune,** **type II & type III**	**Different lung involvement**
Antiphospholipid Syndrome	**ACA & other types APL - antibodies**	**Rare are diagnosed at time**
Idiopathic Pulmonary Fibrosis	**Unknown etiology**	**Primary or end - stage of the inflammation in the lung**
Pulmonary Eosinophilic Syndromes	**Elevated Eo in blood and in situ** **Eo>1500/mm^3**	**Pulmonary infiltrates** **9 clinical forms**

hypersensitivity immune responses

All 4 types of Gel and Coombes hypersensitivity diseases are represented in the lung

Type 1	atopic asthma	IgE antibody
Type 2	Goodpasteur's syndrome	IgG anti-basement memb
Type 3	allergic alveolitis	immune-complex disease
Type 4	pulmonary tuberculosis	activated macrophages

protective immune responses

Vaccination

- ***Strep pneumoniae*** **(Pneumovax)**
- ***Bordetella pertussis (triple vaccine DPT)***
- ***Haemophilus influenzae B (Hib vaccine)***
- ***Neisseria meningitidis C***
- **BCG**
- ***Corynebacterium diphtheriae (anti-toxin)***
- **Influenza**

Immunologic Methods for Diagnosis in Lung Diseases

blood (serology) – C3, C4, C1-IHN, Ig (G, A, M), IgE, CRP, a 1-AT, autoantibodies, infections diseases

blood (cells) - CMI - ab gd CD3, CD4, CD8, CD19, NK, adhesion molecules CD62L, CD11b, CD54, CD25, CD86

cutaneous tests – test for type 1 allergic reaction; MULTITEST® CMI (Skin Test Antigens for Cell-Mediated Immunity); Mantu test

invasive methods - bronchoscopy, pleural punction - respiratory cells profile in BALF and PF

biopsy - histological examination, immunohistochemial staining