THE LYMPHATIC SYSTEM

PART 3 – THE LYMPHATIC SYSTEM AND IMMUNITY

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This third article in a four-part series on the lymphatic system discusses its role in immunity, which it fulfils by trapping foreign material and presenting it to the leukocytes (white blood cells) of the immune system.

COMMON ROUTES OF INFECTION
Potential pathogens can enter the body via a variety of routes:
- The skin (via direct contact, particularly if the epidermis is broken by injuries);
- The respiratory system (via inhalation);
- The gut (via ingestion);
- The genitourinary tract.

Like most areas of the body, each of these systems contains a dense network of lymphatic capillaries (see part 1 of this series). It is therefore inevitable that pathogenic material will end up circulating within the lymphatic system.

To remove potential pathogens, the body produces phagocytic antigen-trapping cells (fig 1), collectively referred to as the reticuloendothelial system (RES) (Ganong, 2001). The cells of the RES are capable of phagocytosis, which literally means cell eating.

All cell surfaces contain small molecules, usually proteins or carbohydrates, known as antigens. Phagocytic cells recognise pathogens as foreign bodies by their antigens, and respond by engulfing them. Phagocytosis allows the RES to trap foreign cells such as bacteria, which are killed by intracellular digestion. Foreign antigens also trigger the production of antibodies, which bind to and effectively label pathogens for destruction by the body’s immune cells.

MAJOR COMPONENTS OF THE RES
The RES has four major components:
- Lymph nodes;
- The spleen;
- Mucosa-associated lymphoid tissue (MALT) including gut-associated lymphoid tissue (GALT), bronchus-associated lymphoid tissue (BALT) and the palatine, lingual and pharyngeal tonsils;
- A variety of specialised fixed phagocytes including Kupffer cells (throughout the liver), Langerhans/dendritic cells (skin), dust cells (alveoli) and microglial cells (brain).

MALT is positioned to protect the respiratory and gastrointestinal tracts from invasion by microbes. The tonsils are aggregates of lymphatic tissue located in the pharynx (palatine), oral cavity (lingual) and nasal cavity (pharyngeal, or adenoids). The tonsils themselves are therefore at a high risk of infection and inflammation (tonsillitis).

Lymph nodes
The lymph nodes appear to play the major role in trapping foreign material. Although they vary in size, each has a characteristic internal structure (fig 2).

Each node is supplied by one or more afferent lymphatic vessels, which deliver lymph from neighbouring tissues. A healthy node will remove the majority of pathogens before the lymph leaves via one or more efferent lymphatic vessels (Marieb, 2006).

Lymph nodes are also supplied with blood via small arteries, which deliver a variety of leukocytes to populate the inner regions of the node. When infection is present, nodes become increasingly active and their oxygen requirements increase.

A vein carries deoxygenated blood away from each node and returns it to the major veins. In times of infection, this venous blood may carry a variety of chemical messengers (cytokines) produced by the leukocytes within the node. These cytokines alert the body to the potential threat as well as triggering a variety of specific immune reactions.

Lymph nodes are divided into several regions (fig 2), and their structure is similar to that of the spleen (see part 2 of this series).
- Fibrous capsule: this forms a protective outer sheath and has processes (trabeculae) that extend into the node, subdividing it into compartments;
- Outer (nodular) cortex: this consists of follicles that are rich in B-lymphocytes (antibody-producing cells). When pathogens are present, these expand, and prominent germinal centres that contain actively dividing, antibody-secreting B-lymphocytes become visible (Doan et al, 2007);
Inner cortex (paracortex): this is just below the outer cortex and is particularly rich in T-lymphocytes, which also continually circulate throughout most other regions of the node. (T-lymphocytes include helper T cells and cytotoxic T cells, cells capable of mounting complex immune responses);

Medulla: the central inner portion contains large numbers of fixed phagocytic macrophages, which monitor the lymph for foreign (potentially pathogenic) material which they phagocytose on contact.

Immune reactions within lymph nodes

The lymph nodes play host to a series of complex cellular interactions that typically lead to the production of specific antibodies. These are centred around fixed macrophage populations (Fig 3). On exposure to a potential pathogen, such as a bacterium, the fixed macrophages engulf the bacterium by phagocytosis then digest it, preventing further bacterial replication. Pieces of the digested bacterium are ‘presented’ on the surface of the macrophage to circulating T-lymphocytes, which become activated and produce a cocktail of cytokines. These stimulate the B-lymphocytes to divide and produce specific antibodies against the offending bacteria (Shier et al, 2006).

After the process described above, some noticeable physiological effects may occur.

- Lymph node swelling: as the antibody-producing B-lymphocytes proliferate, the affected lymph nodes enlarge and may become palpable and tender;
- Fever: some of the cytokines released are pyrogenic (cause fever) and act directly on the thermoregulatory centre within the hypothalamus to raise body temperature. Since most human pathogens divide optimally at around 37°C, this slows bacterial replication and allows the immune system to deal with the infection more efficiently.

CLINICAL EXAMINATION

Both swollen lymph nodes and fever are signs that the body is mounting an effective immune response. The fact that lymph nodes are so efficient at trapping pathogenic material can be used to trace the origins of infections by checking for swelling:

- Cervical lymph nodes/tonsils usually indicate upper respiratory tract infections;
- Axial lymph nodes usually indicate lower respiratory tract infections, or lung or breast cancer;
- Mammary plexus nodes usually indicate mastitis or breast cancer;
- GALT – also known as Peyer’s patches – usually indicates gastrointestinal disturbances, infections and malignancies;
- Inguinal lymph nodes usually indicate infections and malignancies of the reproductive system, urinary system and the colon.

METASTATIC SPREAD OF MALIGNANCY

Because virtually all areas of the body are infiltrated by lymphatic vessels, tumours undergoing metastatic fragmentation can readily spread to other regions of the body via the lymphatic system (Seeley et al, 2006). It is common for a primary tumour to quickly establish secondary spread in the neighbouring lymph nodes – for example, breast cancer is often followed by secondary involvement of the axial lymph nodes.

Malignant involvement of the lymph nodes often leads to obstruction of lymphatic flow and sometimes complete occlusion of the lymphatic vessels. This can cause a ‘backing up’ of lymph and swelling of the elastic lymphatic vessels (lymphoedema), which is discussed in part 4 on pathologies of the lymphatic system.

REFERENCES


