Table 3-7 Role of Mediators in Different Reactions of Inflammation

Reaction of Inflammation	Principal Mediators
Vasodilation	Histamine Prostaglandins
Increased vascular permeability	Histamine and serotonin C3a and C5a (by liberating vasoactive amines from mast cells, other cells) Leukotrienes C_4, D_4, E_4
Chemotaxis, leukocyte recruitment and activation	TNF, IL-1 Chemokines C3a, C5a Leukotriene B_4
Fever	IL-1, TNF Prostaglandins
Pain	Prostaglandins Bradykinin
Tissue damage	Lysosomal enzymes of leukocytes Reactive oxygen species

blood pressure, stimulation of hormone secretion by endocrine cells, and increasing vascular permeability.

When Lewis discovered the role of histamine in inflammation, one mediator was thought to be enough. Now, we are wallowing in them! Yet, from this large compendium, it is likely that a few mediators are most important for the reactions of acute inflammation in vivo, and these are summarized in Table 3-7. The redundancy of the mediators and their actions ensures that this protective response remains robust and is not readily subverted.

KEY CONCEPTS

Actions of the Principal Mediators of Inflammation

- Vasoactive amines, mainly histamine: vasodilation and increased vascular permeability
- Arachidonic acid metabolites (prostaglandins and leukotrienes): several forms exist and are involved in vascular reactions, leukocyte chemotaxis, and other reactions of inflammation; antagonized by lipoxins
- Cytokines: proteins produced by many cell types; usually act at short range; mediate multiple effects, mainly in leukocyte recruitment and migration; principal ones in acute inflammation are TNF, IL-1, and chemokines
- Complement proteins: Activation of the complement system by microbes or antibodies leads to the generation of multiple breakdown products, which are responsible for leukocyte chemotaxis, opsonization, and phagocytosis of microbes and other particles, and cell killing
- Kinins: produced by proteolytic cleavage of precursors; mediate vascular reaction, pain

Morphologic Patterns of Acute Inflammation

The morphologic hallmarks of acute inflammatory reactions are dilation of small blood vessels and accumulation of leukocytes and fluid in the extravascular tissue. However, special morphologic patterns are often superimposed on these general features, depending on the severity of the reaction, its specific cause, and the particular tissue and site involved. The importance of recognizing the gross and microscopic patterns is that they often provide valuable clues about the underlying cause.

Serous Inflammation

Serous inflammation is marked by the exudation of cell-poor fluid into spaces created by cell injury or into body cavities lined by the peritoneum, pleura, or pericardium. Typically, the fluid in serous inflammation is not infected by destructive organisms and does not contain large numbers of leukocytes (which tend to produce purulent inflammation, described later). In body cavities the fluid may be derived from the plasma (as a result of increased vascular permeability) or from the secretions of mesothelial cells (as a result of local irritation); accumulation of fluid in these cavities is called an *effusion*. (Effusions also occur in noninflammatory conditions, such as reduced blood outflow in heart failure, or reduced plasma protein levels in some kidney and liver diseases.) The skin blister resulting from a burn or viral infection represents accumulation of serous fluid within or immediately beneath the damaged epidermis of the skin (Fig. 3-13).

Fibrinous Inflammation

With greater increase in vascular permeability, large molecules such as fibrinogen pass out of the blood, and fibrin is formed and deposited in the extracellular space. **A fibrinous exudate develops when the vascular leaks are large or there is a local procoagulant stimulus** (e.g., cancer cells). A fibrinous exudate is characteristic of inflammation in the lining of body cavities, such as the meninges, pericardium (Fig. 3-14*A*), and pleura. Histologically, fibrin appears as an eosinophilic meshwork of threads or sometimes as an amorphous coagulum (Fig. 3-14B). Fibrinous exudates may be dissolved by fibrinolysis and cleared by macrophages. If the fibrin is not removed, over time it may stimulate the ingrowth of fibroblasts and blood vessels and thus lead to scarring. Conversion of the fibrinous exudate to scar tissue *(organization)* within the pericardial sac leads to opaque fibrous thickening of the pericardium and

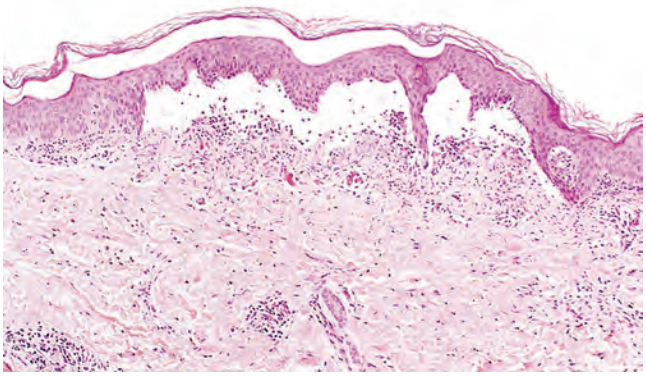

Figure 3-13 Serous inflammation. Low-power view of a cross-section of a skin blister showing the epidermis separated from the dermis by a focal collection of serous effusion.