leukotrienes. Assistance from environ- mental cues (released clotting factors, kininogens, and complement) is critical to the preparation of vascular beds to allow cellular influx.As a class, they are small polypeptides synthesized by a wide variety of cell types, all of which Pathological Consequences of the Inflammatory Response The initiation of the pro inflammatory responses is extremely potent to limit the spread of microorganisms; however, full clearance of the infectious agent typically requires adaptive immune components.The opsonins act as molecular beacons, allowing interaction with receptors on macrophages, monocytes, and neutrophils to enhance phagocytosis and elevate mechanisms of targeted organism destruction.Recognition can occur directly through mannose receptors, scavenger receptors, or Tolllike receptors (TLRs), receptors that detect common pathogenic motifs (pathogen-associated molecular patterns; PAMPs).Proteolytic Pathogen Recognition and Cytokine Signaling Phagocytes bear several unique receptors that recognize microbial components, bind bacterial carbohydrates, and induce phagocytosis.Clotting and formation of a fibrin matrix impede the movement of microorganisms in the local area; generation of breakdown products in the cascading events also attracts and activates incoming leukocytes.Overall, complement and its related components exert multiple biological functions that are critical components of inflammation, including activation and regulation of both innate and adaptive immune functions (Fig.Plasma serine proteases, normally present as inactive molecules, are activated; some of these function to produce kinins to mediate firbrinolytic events, vascular permeability, and sensation of pain.Activation of complement enzymes results in subsequent cleavage of proteins to yield specific polypeptide fragments with short-lived enzymatic functions related to inflammation.Depending on prior exposure or positive vaccination status, there may also be an abundance of specific antibodies reactive to antigenic features present in destructive pathogens.In these enzymatic cascades, complement components bind directly to pathogens via the recognition of bacterial sugars and lipids.Similar to the events described here, the deposition of complement on the invading pathogen leads to a cascade of enzymatic reactions, culminating in pore channel assembly on the organism surface.In addition, internal protein complexes, such as the inflammasome, further the response to the recognition event via internal processing of inactive forms of proinflammatory molecules to produce mature and active mediators.Activation of local response is followed by activity of the lymphatics to functionally drain fluids, cells, and debris to nearby lymph nodes, where phagocytic antigen presenting cells -show?Antibody entry to the area offers multiple functions, the most critical of which resides within the end of the antibody molecule that can recognize unique shapes and forms, with a specific and unique binding site for foreign substances.Antibody recognition of multiple regions on the microorganism can result in a latticework structure, a precipitate, which promotes organism clearance.Two other pathways of complement activation, the alternate pathway and the lectin pathway, function to allow direct lysis of microorganisms in the absence of antibodies.Activation and Directed Migration of Leukocytes One of the most prevalent by-products of the complement enzymatic cascade is the production of molecules with the ability to call in and activate leukocytes.Proteolytic degradation of complement components releases leukocyte chemotactic factors referred to as anaphylatoxins.Dilated local blood vessels, capillaries, and small venules/arterioles subsequently allow fluid (edema) to accumulate in the damaged area.In effect, antibodies recognize toxins and deleterious factors;

recognition results in the inhibition and neutralization of their toxic properties.35 An intracellular vesicle, referred to as the complosome, has a strong impact on cell processes and metabolism, perhaps exerting influence on how the host cell adjusts to the presence of intracellular pathogens.In addition to the PAMP molecules described here, a unique subset of danger-associated molecular patterns (DAMPs), can trigger similar responses.However, there is also a great need for systemic communication that can mediate responses across great distances to direct cells and organs located distant from the site of tissue damage.If the breach in the mechanical barrier is deep enough, damaged blood vessels also directly flood the local area with leukocytes, red blood cells (RBCs), and platelets.Simply coating the agent with antibodies targets it for attack by serum enzymes that comprise the complement cascade (Fig.The complement components may be circulating in the blood, may be expressed on cell surfaces, and may even be found as intracellular-residing proteins.Synthesis of this structure culminates in a pore channel, called a membrane attack complex (MAC), which causes osmotic lysis of the pathogen or infected cell.Indeed, we will see in later chapters that the direct interaction of cells that initiate the proinflammatory response with incoming lymphocytes triggers adaptive cell activity.Cell-to-cell contact gives the advantage of directly delivering cytokines and mediators, allowing functional lymphocyte development in the immediate area to target productive immune function.Chemokines assist in leukocyte .(migration into tissue (diapedesis).Fig. 2.2). 2.3