Basophils in Human Disease

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The basophil, first described by Paul Ehrlich in 1879, is now recognized as one of the circulating granulocytes derived from the same bone marrow precursors as eosinophils and neutrophils. Basophils differentiate in the bone marrow and are normally found in the circulation and not in the extravascular tissues. Basophils comprise 0.5–1.0% (20–45 cells/mm³) of the circulating leukocytes and are thus the least common human granulocyte. Basophils are distinguished from mast cells by being smaller (10–14 μm), having a segmented nucleus and larger metachromatic cytoplasmic granules (1.2 μm, though variable) that stain less intensely. Mast cells also originate in the bone marrow, but their precursor leaves the marrow, enters the tissues, and slowly differentiates into a mast cell over 3–4 months. Basophils are thought to have a short half-life (2.5 days in a patient with basophilic leukemia). In humans, basophils contain almost all of the blood histamine. The frequency of basophils varies in different species, and usually an inverse relationship between mast cell and basophil frequency exists. Interestingly, in some lower vertebrates such as chickens, a single-cell type with metachromatic staining granules exists in both the circulation and in the tissues. A very close relationship appears to exist between the function of mast cells and basophils; the mast cell being a normal component of the tissues and the basophil being a similar, but intravascular circulating cell that can be recruited into the tissue by immunological mechanisms.

The basophil appears to be involved in a wide variety of immune-inflammatory disease states. Release of histamine from the blood basophils of allergic patients has served as an excellent in vitro assay of immediate hypersensitivity for many years, but knowledge of the actual participation of basophils in allergic diseases has come about only recently through an appreciation of the fact that significant tissue infiltrates of basophils accompany some of these diseases and, in fact, they often represent a manifestation of overlapping delayed-type hypersensitivity responses.
Immediate Hypersensitivity

Immediate hypersensitivity reactions usually occur after the interaction of antigen and specific IgE antibody attached via its Fc portion to Fc receptors on the surface of mast cells. Typically, allergic atopic diseases have a major immediate hypersensitivity component. Thus the early symptoms after allergen exposure in allergic rhinitis, asthma, urticaria, anaphylaxis, food allergy, drug allergy, and to a lesser extent atopic dermatitis, can be considered IgE-dependent and mast cell-mediated events. In allergic rhinitis, the offending agent is often an environmental inhalant allergen to which the patient has mounted an immune response in which IgE production is prominent. In general, the apparent clinical signs of allergic disease are dependent upon the organ system involved, the properties of the allergen, its dose and route of administration, previous exposure either naturally or as part of a therapeutic regime, and other host factors. When specific IgE antibody interacts with allergen, there is aggregation of Fc receptors that results in anaphylactic degranulation with granule content extrusion from either the mast cell or the basophil. This results in the liberation of mediators, both preformed and newly synthesized, that orchestrate the inflammatory response that develops. Smooth muscle contraction, vascular dilation, and vessel permeability all develop, in addition to recruitment of infiltrating leukocytes.

Because basophils are normally found only in the circulation or in the bone marrow, they are involved in immediate hypersensitivity responses that are systemic in nature. These responses, called systemic anaphylactic reactions, involve massive basophil and mast cell degranulation with generalized systemic release of mediators. These events are probably associated with activation of the complement, kinin, and clotting cascade mechanisms. Symptoms include those of vascular collapse and changes in particular target (shock) organs. The skin, larynx, trachea, esophagus, eyes, and periorbital region are frequently involved. Drugs, foods, and insect stings are among the most frequent causes of such reactions. Interestingly, elevated plasma histamine levels occur with the hemodynamic changes of anaphylaxis associated with hymenoptera sensitivity, but not with the systemic urticarial response alone. The former may be due to combined degranulation of blood and bone marrow basophils or tissue mast cells releasing vasoactive amines in sufficient quantity to cause vascular collapse, but the latter may just represent systemic cutaneous degranulation of mast cells.

Anaphylactoid reactions represent immediate-type systemic responses in which basophils and/or mast cells are also degranulating, but IgE antibodies or other immunological mechanisms of activation are not the cause. The radiocontrast media reaction is an example of this. A number of mechanisms have been proposed including leukocyte histamine release induced directly by radioconstant media and complement activation. Likewise, carbohydrates such as Dextran and Mannitol and certain dyes such as bromosulphothalein can induce anaphylactoid reactions, presumably by direct activation of basophils and/or mast cells.

Mast cells and basophils are probably not the only cells involved in immediate reactions; neutrophils can produce mediators such as platelet acti-