Who is the father of innate immunity?

The thermometer can show that something is wrong with a patient (pyrexia). But it cannot be more specific. Likewise, there is evidence, dating back to the ancient Greeks, that the slight changes in blood serum that occur when a person is ill cause the red cells in that blood to clump together and settle rapidly. Supplementing the thermometer, this “erythrocyte sedimentation rate” (ESR) test, acts as a general indicator of ill-health. Around 1900 another, relatively non-specific, health indicator was identified by a London physician, Almroth Wright, upon whom was based a character in Shaw’s play *The Doctors Dilemma* (Fig. 1). He showed that serum can act to “butter” intruding bacteria. This buttering favours their ingestion by scavenging cells (phagocytes), a process often accompanied by the unsheathing of another serum component (the complement “dagger”).

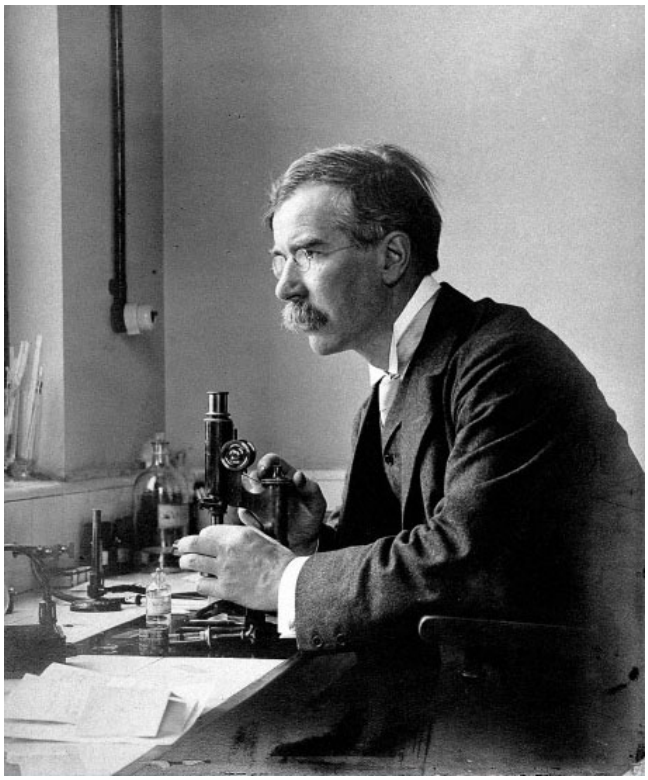

Fig. 1. Almroth Wright in his laboratory. Wellcome Images Library, London.

Wright acknowledged the earlier studies of Paul Ehrlich on antibodies and complement, and of Elie Metchnikoff on phagocytes. However, since the “buttering” increased in the early hours of infection, it appeared as an inherited ability (*innate immunity*) that preceded Ehrlich’s more specific antibody response (*acquired immunity*). This later-developing response could precisely target distinct microorganisms and then unsheath what became known as the classical pathway of complement activation.

Wright's work was unknowingly rediscovered by US immunologist, Charles Janeway (1943-2003), who was hailed in an obituary in *The Lancet* as the "father of innate immunity." Metchnikoff (1845-1916) was hailed similarly in *Cell* (August 2016). But Forsdyke in *Microbes & Infection* (August 2016) ascribes paternity to Wright. The discovery in 1970 of complement activation by a plant protein ("lectin") that bound to cell surface sugars (mannose), was followed by molecular identification of serum opsonins (e.g. mannose-binding lectins; MBLs) and analysis of their buttering mechanisms. These opsonins are rapidly released from the liver when normal body barriers to infection (e.g. skin) are overcome and, as with the classical pathway, they can unsheathe complement (Fig. 2).

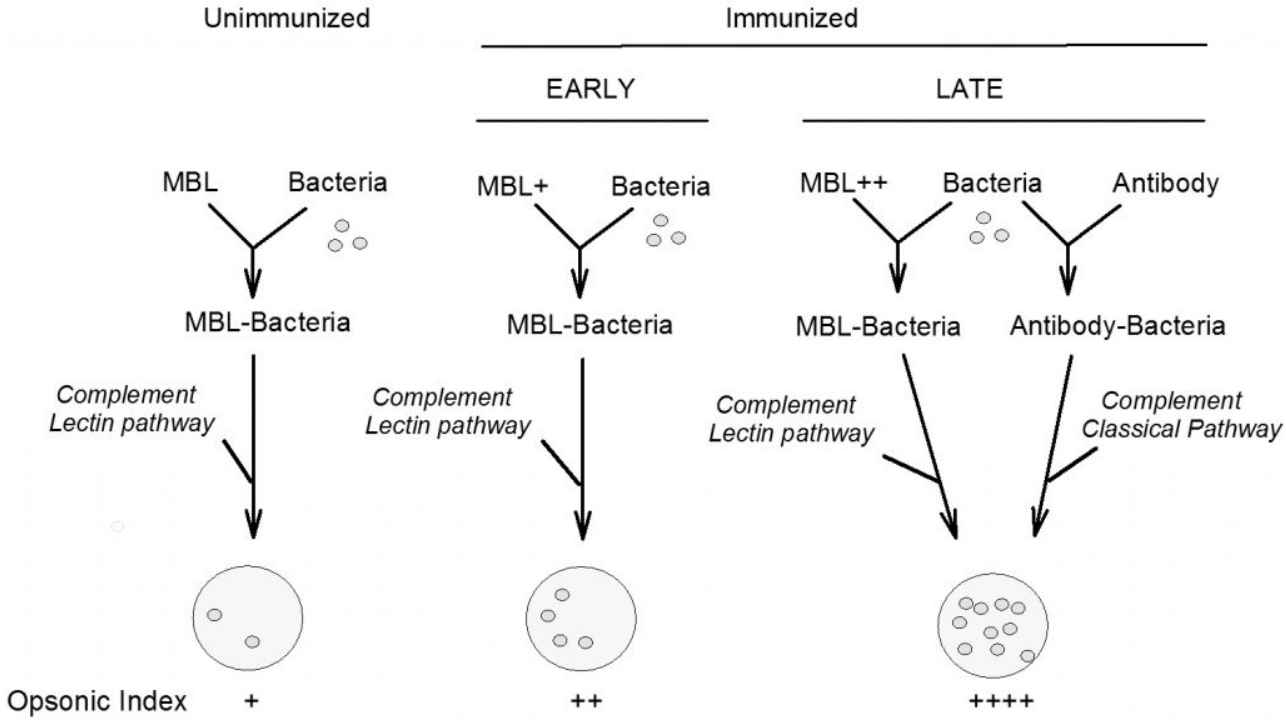

Fig. 2. Progressive "buttering" of bacteria (small circles) by MBL and/or antibody, and their ingestion by phagocytes (large circles), as measured by the "opsonic index" at different stages of a primary immune response.

Thus, as Wright well appreciated, against potential microbial aggressors there are three sequential lines of defence: skin, *innate* immune response (MBL and lectin pathway), *acquired* immune response (antibody and classical pathway).

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