Streptococcus pneumoniae (pneumococcus) is a commensal bacterium that is transmitted between humans by aerosol. Colonisation of the nasopharynx occurs, but does not usually cause disease in healthy individuals. However, in young children, the elderly and immunocompromised individuals, particularly HIV-infected, invasion of other body compartments can occur leading to infections such as pneumonia, otitis media, meningitis, encephalitis and systemic bacteraemia.
A common dissemination route, particularly in young children, is ascent of bacteria through the Eustachian tube to the middle ear causing otitis media. Prolonged infection in this compartment can permit spread of bacteria into the CSF through the mastoid sinuses leading to meningitis.
A common route of dissemination from the nasopharynx, particularly in adults, is invasion of the lungs causing pneumonia. Inflammation of the lungs can permit escape of bacteria into the bloodstream. Entry of bacteria into the systemic blood system can cause bacteraemia, but can also lead to invasion of the CSF through capillaries that traverse the choroid plexus or subarachnoid space, causing meningitis. Bacteria may also cross the blood-brain barrier into the CNS causing bacterial encephalitis, but this is less common.
Dissemination to the bloodstream, meninges and brain

Alternatively, penetration of bacteria into the nasopharyngeal submucosa by translocation across the epithelium can occur. In turn, this can lead to translocation of bacteria across the endothelium of blood capillaries causing bacteraemia. Once in the bloodstream, bacteria can cross the endothelium and enter the CSF through the blood vessels traversing the choroid plexus or subarachnoid spaces, causing meningitis. Endothelial cells of the blood-brain barrier can also be penetrated allowing bacterial spread into the CNS causing encephalitis.
Anti-capsular antibodies play an important role in control of *Streptococcus pneumoniae*. B lymphocytes in the submucosa secrete IgM and dimeric IgA which is transported across the epithelium of the upper respiratory tract by transcytosis. The polymeric immunoglobulin receptor (PigR), expressed on the basolateral membrane of epithelial cells, binds to the J chain of IgM and dimeric IgA. The bound antibodies are then transported in a vesicle through the cell and released at the apical membrane. Proteosomal cleavage of the receptor at the membrane surface releases the antibody and leaves the secretory component still attached.
Streptococcus pneumoniae expresses a surface protein, PspC, that facilitates translocation of bacteria by reverse transcytosis through upper respiratory epithelial cells. This is achieved by PspC binding to the polymeric immunoglobulin receptor (PigR) which normally transports IgM and dimeric IgA to the mucosal surface. Although primarily expressed at the epithelial basolateral cell surface, PigR is found at a low level on the apical membrane. Binding of bacterial PspC to the secretory component of PigR induces reverse transcytosis that delivers intact bacteria into the submucosa.
Immune responses against bacteria present in the submucosa of the upper respiratory tract promotes the release of inflammatory cytokines that upregulate the expression of cell surface receptors on capillary endothelial cells. One of these receptors is the platelet activating receptor (rPAF). *Streptococcus Pneumoniae* expresses a cell surface protein ChoP that binds to rPAF. Engagement of rPAF triggers clathrin-dependent endocytosis of the receptor-complex which facilitates internalisation of the bound bacteria. Escape into capillary lumen can then occur through the apical membrane of the endothelial cell.
Translocation across the blood-brain barrier

Invasion of the bloodstream causes bacteraemia. Systemic inflammatory responses upregulate surface expression of endothelial cell receptors, such as platelet activating factor receptor (rPAF). *Streptococcus pneumoniae* expresses ChoP on the bacterial cell surface that binds rPAF and induces clathrin-mediated internalisation. Escape of bacteria through the basolateral membrane promotes invasion of the CNS causing bacterial encephalitis. More commonly, the same mechanism permits bacteria to invade the CSF from the capillaries that traverse the choroid plexus and the subarachnoid space, causing meningitis.