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# OA011-04. Striking elevations in systemic and mucosal cytokine and chemokine levels in acute HIV-1 infection

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## Background

Innate immune responses can be activated rapidly in response to infection and may contribute to control of early viral replication or conversely, mediate immunopathogenic effects. To gain insight into the nature and kinetics of the earliest cytokine responses activated in acute HIV-1 infection (AHI), we analysed changes in systemic and mucosal cytokine/chemokine levels during primary infection.

## Methods

Cytokine/chemokine levels were measured by Luminex and ELISA in sequential blood plasma samples collected during the eclipse and exponential viral expansion phases from US plasma donors acquiring HIV-1 infection, and in blood plasma, cervicovaginal lavage (CVL) and seminal plasma timecourses from CHAVI 001 AHI subjects (typically spanning the time from peak viraemia to early infection), plus HIV-seronegative controls.

## Results

The increase in viraemia in AHI was associated with rapid activation of a striking systemic cytokine cascade, including rapid and transient elevations in IFNalpha and IL-15, rapid and more sustained increases in TNFalpha, IP-10 and MCP-1, more slowly-initiated elevations in additional pro-inflammatory factors including IL-6, IL-8, IL-18 and IFNgamma and a late-peaking increase in IL-10. Most analytes returned to baseline as viraemia declined, but low-level elevations in some factors were sustained into early infection. Multiple cytokines/chemokines were transiently elevated in CVL during AHI. Some, e.g. TNFalpha, IL-1beta and IL-8, were typically already highly elevated in CVL at the earliest timepoint studied (even prior to peak viraemia), suggestive of a local pro-inflammatory response preceding systemic immune activation. Others, e.g. IFNgamma, MIP-1beta and IL-10 were only elevated in CVL around peak viraemia. Modest elevations in seminal plasma cytokine/chemokine levels occurred in AHI in parallel with systemic analyte increases.

## Conclusion

Although some individual cytokines may have beneficial effects, the intense cytokine storm in AHI may have immunopathological consequences, promoting immune activation, viral replication and CD4+ T cell loss, and could be a target for vaccine-induced down-modulation.