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# Therapeutic apheresis in transition: New indications and the emergence of precision apheresis

Over the past decade, therapeutic apheresis has moved well beyond its established role in autoimmune, hematologic, and neurologic disease. Two forces are driving this expansion. The first is the growing recognition that circulating mediators—autoantibodies, immune complexes, inflammatory cytokines, atherogenic lipoproteins, and protein-bound toxins—contribute to a widening range of conditions, making their removal a rational therapeutic strategy. The second is technological: a shift away from the wholesale removal of plasma and toward the selective extraction of specific pathogenic components. Together, these developments mark a transition from apheresis as a rescue intervention toward what may be called precision apheresis. This theme issue brings together four contributions that map that transition across neurodegeneration, post-infectious immune dysregulation, cardiovascular and renal disease, and the technological frontier.

The clearest signal that apheresis can address a disease long considered beyond its reach came from the AMBAR study, which demonstrated that therapeutic plasma exchange (TPE) with albumin replacement slowed cognitive and functional decline in patients with moderate Alzheimer's disease [1]. In the opening article, Khatri traces the use of TPE in Alzheimer's disease from that controlled trial through the accumulating real-world experience that has followed, and situates it within a contemporary, systems-biology view of the disease in which a broadly acting intervention may complement, rather than compete with, selective anti-amyloid antibodies [2].

The COVID-19 pandemic introduced the world to a spectrum of post-acute illness arising not only from the virus itself but from the immune response to it—and, in some cases, even from vaccination. These presentations echoed syndromes recognized long before, including the chronic symptoms that can follow Lyme disease, myalgic encephalomyelitis/chronic fatigue syndrome, and the pediatric PANS/PANDAS phenotypes. Kaplan reviews the evidence for immune dysregulation across these post-infectious syndromes and the rationale for immunomodulatory therapy, including TPE [3]. A recurring lesson runs through this work: unselected populations are unlikely to benefit, and biomarker-guided patient selection is essential to define where apheresis has a role.

While TPE remains the most widely used modality, removing the entire plasma compartment is neither always necessary nor always desirable, and it carries the cost and logistical burden of replacement fluid. The remaining two articles turn to selective removal. Nadim and Akgun examine lipoprotein apheresis—a mature, decades-proven precision technique—across its established role in familial hypercholesterolemia and elevated lipoprotein(a) and its emerging applications in peripheral arterial and renal disease, where the procedure contributes to cardiovascular and renal risk reduction through mechanisms that extend beyond lipid lowering [4].

Finally, Kiprov et al. describe the technological frontier: selective plasma adsorption using the MTx.100 column, which removes pro-inflammatory cytokines, protein-bound waste, and environmental toxins while preserving immunoglobulins, coagulation factors, and the patient's own plasma [5]. They frame this within the broader concept of subtractive precision medicine—the targeted removal of disease-contributing substances as a complement to additive pharmacotherapy.

Read together, these articles describe a field moving from broad to selective, and from empiric use toward mechanistically grounded, phenotype-driven application. The guidelines of the American Society for Apheresis continue to anchor practice as new indications are evaluated [6]. The central challenge ahead is the one each contribution identifies in its own domain: to match the right patient—defined increasingly by biomarkers and mechanism—to the right form of removal. That is the promise of precision apheresis, and the purpose of this issue.

## Declaration of Generative AI and AI-assisted technologies in the writing process

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## Conflict of Interest

D.D. Kiprov is the founder and owner of Global Apheresis Inc., and serves as Chief Medical Officer of Marker Therapeutics AG (the manufacturer of the MTx.100 column) and of Clarify Clinics, with executive consulting roles at other medical organizations. A.P. Green declares no conflicts of interest.

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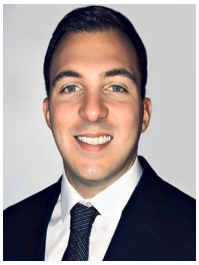

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