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Biological sex impacts transplant outcomes

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Abstract – Biological sex impacts transplant outcomes Biological sex impacts afferent and efferent immune responses in a profound and multi-faceted fashion, with sex-specific effects and outcomes demonstrated for many diseases. Notably, there is a strikingly higher incidence of major autoimmune diseases in females. Sex-specific outcomes have also been recognized for various oncological, cardiovascular, and infectious diseases including COVID-19. Moreover, responses to vaccines and immunotherapies are impacted by biological sex. Of note, sex-specific alloimmune responses have been considered as early as 1950 by Billingham, Brent and Medawar in experimental skin transplantation models. Nevertheless, more detailed work on clinical effects and mechanisms in either experimental or clinical transplantation have not been undertaken. Recent clinical studies have shown that donor and recipient sex independently impact transplant outcomes, effects that are further modified by aging. Clinical and experimental data have also shown that donor and recipient sex affect alloimmune responses on various levels. While those effects are recognized, further insights into mechanistic details are necessary to implement sex-specific treatments. There is also growing recognition that a focus on sex-based differences as a result of genetic and hormone profiles can increase the rigor of scientific inquiry while enhancing enhance the validity of research. Likewise, there is a necessity to confirm critical experimental findings in both sexes. While the complexity of those requests is recognized, analyzing sex-specific outcomes and alloimmune responses will enhance consistency and value of basic and clinical research. Here, we summarize relevant findings in immunity in addition to studies in clinical and experimental organ transplantation detailing effects of biological sex on alloimmunity. Understanding both clinical impact and mechanisms is expected to provide critical insights on the complexity of alloimmune responses with the potential to fine-tune treatment and allocation while providing a rationale to include both sexes in transplant research.