

BACKGROUND

- A global shortage of human donor organs results in long waitlists and increasing mortality for patients with end-stage organ failure
- Alternative options for life-saving organ transplantation are needed
- Xenotransplantation is an emerging option
- Recent advancements in donor porcine genomic alterations have allowed clinical xenotransplantation in advanced cardiac and renal failure
- Despite progress, infectious disease hazards and their potential impacts on public health remain a concern

WHAT IS XENOTRANSPLANTATION?

Any procedure that involves the transplantation or transfer of living cells, tissues, or organs from an animal to a human

PURPOSE OF THE REVIEW

- To synthesize current knowledge on the **public health implications** arising from the **infectious disease risks** associated with pig-to-human xenotransplantation at scale

INFECTIOUS DISEASE HAZARDS

may be categorized: **taxonomically**; according to **temporality of potential exposure** and/or **reactivation**; and according to **anthroponotic versus zoonotic** transmission

MAJOR INFECTIOUS DISEASE HAZARDS

- ! Organisms endogenous to **donor** and potentially *zoonotic* (known and unknown)
- ! Organisms endogenous to **recipient** with potential for *exacerbation* and/or *reactivation*
- ! Organisms that are an **increased risk to recipient** due to added levels of *immunosuppression* after xenotransplantation (known and unknown)

WHAT HAVE CLINICAL CASES TAUGHT US?

- Recent clinical cases of pig-to-human cardiac and renal xenotransplantation have provided insights into infectious organisms that may contribute to xenograft rejection and the associated cascade of inflammatory responses
- A full understanding of how endogenous porcine viruses may interact with recipient tissues and impact clinical outcomes has yet to emerge
- Based on the evolution of gene-edited donors, xenosis due to endogenous porcine viruses seem surmountable

IMPACT OF IMMUNOSUPPRESSION AT SCALE

- Impacts of immunosuppression-at-scale will be differentially borne by those most affected by reactivating infections i.e. **tuberculosis**, **hepatitis B**, and **strongyloidiasis**
- These may differentially impact those living in rural poverty, who live in crowded regions, areas with poor sanitation, undernutrition, and economic disenfranchisement
- **Chagas disease** and **leishmaniasis** also have a possibility of reactivation and differentially affecting people in the global South

STRONGYLOIDIASIS

- Risk of reactivation is high
- Significant risk of false negative diagnostic testing leading to increased burden of untreated disease
- Untreated cases need inpatient admission and ICU-level care

CHAGAS DISEASE

- Immunosuppression increases risk of reactivation
- More infected individuals can transmit parasite to others
- Treatment of disease is less effective in asymptomatic people and inaccessible and expensive

LEISHMANIASIS

- Patients with relapsing visceral form can transmit parasite to vector in densely populated endemic areas
- Immunosuppression could lead to severe infection

REFERENCES

