CHRONIC KIDNEY DISEASE

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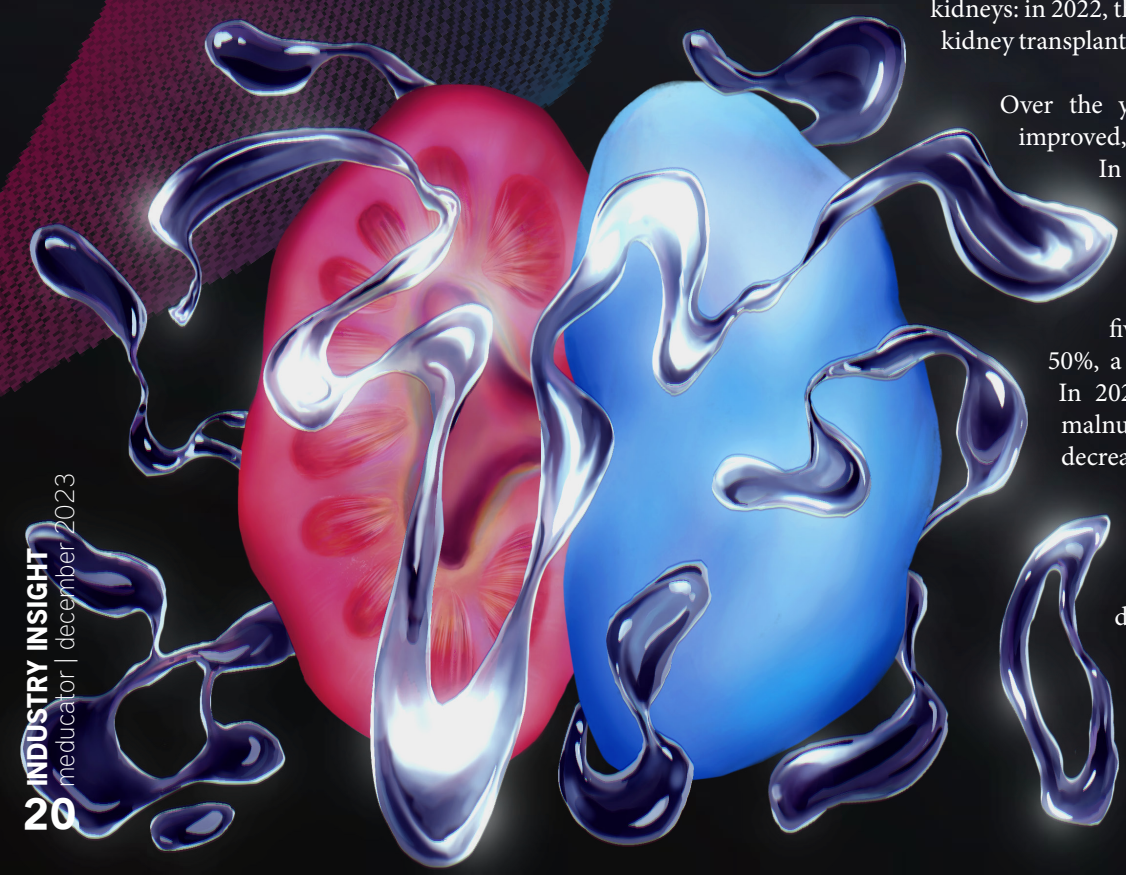
WHAT IS CHRONIC KIDNEY DISEASE?

Chronic kidney disease (CKD) is defined as low filtration function in the kidneys, protein in the urine, or functionally-important structural abnormalities.[1] Low filtration function is associated with waste build-up in the bloodstream and difficulty in excreting salt and water, leading to fluid build-up.[1] CKD may worsen over time, and some individuals with CKD may experience kidney failure, at which point dialysis or transplantation is required to replace kidney function.[1]

CKD may be caused by diabetes, renovascular disease, glomerulonephritis, polycystic kidney disease, and various genetic and environmental factors. In 2023, approximately four million Canadians live with and 11-13% of the global population are affected by CKD.[2] This disorder has a 50% five-year mortality rate and is associated with lower quality of life compared to other chronic diseases, including sickle cell anemia, cancer, and cystic fibrosis.[3] CKD's comorbidities, such as diabetes, are increasing in prevalence and can increase the risk of developing CKD.[3] Thus, the rates of CKD are also set to rise.[3] Annual CKD management costs across Canada total $40 billion, with dialysis treatment for people with end-stage kidney disease (ESKD) costing $100,000 per patient.[3]

CURRENT TREATMENTS

Current treatments for ESKD include hemodialysis, peritoneal dialysis (PD), and kidney transplantation.[4] Hemodialysis can be used to replace kidney function by filtering a patients' blood to remove urea, salts, and other toxins. This process is intrusive and resource-intensive, involving three to four hour sessions three times a week. PD is a less resource-intensive home-based modality associated with less fluctuation in fluid status and provides similar life expectancy but better wellness outcomes.[4] PD works by adding and removing dialysis fluid to the bloodstream via a bag implanted to the peritoneum lining.[5] Kidney transplants surgically replace a malfunctioning kidney with a healthy donor kidney. However, transplants require lifelong immunosuppressive treatment and may eventually fail. Nonetheless, patients who undergo kidney transplantation had a 1.2 in 100 annual death rate compared with 16.5 in 100 for dialysis patients.[6] There is, however, a shortage of kidneys: in 2022, there were 2,813 individuals in need of a kidney transplant in Canada and 1,195 kidneys donated.[7]



Over the years, these techniques have rapidly improved, increasing in efficiency and efficacy. In 1998, the one-year mortality rate of dialysis patients was 25%, primarily due to infection, cardiovascular conditions, and comorbidities, such as high blood pressure.[8] In 2012, the five-year mortality rate was recorded at 50%, a significant improvement from 1998.[9] In 2023, many related conditions such as malnutrition and high blood pressure have decreased due to improvements in dialysis efficiency, quality, and accessibility. During the same timeframe, the 10-year survival rate for recipients of kidney transplant from deceased donors increased from 60.5% to 66.9%.[8,9] The long-term negative effects of kidney grafts likewise decreased due to the refinement of immunosuppressive therapies.

ASTRAZENECA

AstraZeneca, partnering with Columbia University, investigated genetic markers of CKD enabling researchers to determine a genetic diagnosis in 10% of CKD patients.[11] AstraZeneca is currently developing genomic databases to identify urinary biomarkers for CKD to create more efficient screening tools. Furthermore, new target treatments are being tested with organ-on-a-chip and 3-D bioprinted models, which can simulate the anatomy and physiology of a real kidney. Subsequently, researchers can conduct more accurate and reliable preliminary testing while reducing some of the financial and physical burden of traditional *in vivo* testing.

Ionis Pharmaceuticals licensed ION532, a drug targeting a prominent genetic driver for kidney disease gene APOL-1, to AstraZeneca for $30 million USD for commercialization.[12,13] ION532 has not yet been clinically tested, but has secured an additional $30 million USD investment upon development.[14]

BAXTER

Healthcare company Baxter International and medical device company Theranova launched an expanded hemodialysis (HDx) treatment, which reportedly "filters a wider range of molecules from the blood than conventional hemodialysis."[15] HDx combines specific filtration techniques to resemble a kidney's natural function.[16] Baxter's post-hoc found that HDx reduced hospitalization rates by 45%, resulting in a $6,098 USD reduction in associated costs per patient. Compared to the most medically effective non-expanded hemodialysis treatment available, the cost of dialysis with Thernaova's HDx was on average $4,772 USD lower per patient.[17]

UNITED THERAPEUTICS

A promising treatment for ESKD is xenotransplantation, which is currently being researched by United Therapeutics (UT).[18] Xenotransplantation involves transplanting cells or organs across different species. Pigs have been identified as the most acceptable donor species for humans, and significant progress is made in modifying the porcine genome to reduce immunological barriers and incompatibilities between pigs and humans.[19] Given that organ transplant supply remains relatively stable while demand increases annually, xenotransplantation could potentially address unmet needs by providing a renewable source of lifesaving organs.[19]

Current research focuses on assessing function and xenograft rejection. Montgomery et al. observed promising results in the prognosis of transplanted kidneys from genetically modified pigs supplied by UT into two human recipients who were declared neurologically dead.[18] Moments after reperfusion, the xenografts in both recipients began to produce urine. The measured platelet, white blood cell counts, and inflammatory markers at various time intervals remained stable and within normal ranges.[18] These results support the viability and potential clinical value of xenotransplantation, providing alternatives to transplants and reducing organ shortages in CKD.[18] As of March 2023, UT funded Johns Hopkins' researcher and surgeon Dr. Kazuhiko Yamada and Dr. Andrew Cameron with $21.4 million USD to perform pre-clinical research and study the outcomes of xenotransplantation in living patients.[19]

QIDNI

Qidni Labs, a Kitchener-based startup, is working on addressing the accessibility of dialysis machines to improve CKD patient outcomes in rural areas, disaster zones, and emergency settings.[20] While traditional dialysis requires 120 liters of purified water per dialysis, Qidni dialyzers require significantly lower amounts of water.[20] By simultaneously providing equivalent quality, time, and price of dialysis, Qidni has been able to reduce water consumption and address the associated filtration costs by using readily-accessible saline solutions available in pharmacy settings.[20]

Additionally, Qidni has developed implantable bioengineered kidneys that use a nanofiltration system to mimic the organ's function and drain waste products into the bladder. The company founder, Dr. Morteza Ahmadi, successfully tested a prototype in a pig, which utilizes ultrathin nanoporous silicon membranes.[21] In 2013, Ahmadi et al. noted the material's fragility and potential to provoke an immune response, suggesting that the membrane should be coated with a biocompatible material.[21] Qidni Labs continues to research and develop novel implantable maintenance-free portal devices that could free patients from dialysis machines.[21]

THE FUTURE OF CKD

The CKD treatment market continues to focus on research and development of more viable treatments for patients and economies alike. As research and industry innovations in this domain progress, the scientific and economic future for kidney failure treatments is promising.

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