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Establishing a national program of islet transplantation in Australia

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We read with interest the opinion piece by Ricordi and Japour in STAT (August 27, 2019). It is interesting that the development of an appropriate funding pathway for islet transplantation seems to have stalled in the US, when in fact it was the early multicentre trials originating from the US and Canada that were the major stimulus for the procedure elsewhere. In Australia, islet transplantation for severe hypoglycaemia and metabolic instability has been funded via the National Funded Centres (NFC) program since 2012. The NFC program was established by the Australian Health Ministers Advisory Council (AHMAC) to provide access for Australian patients to high cost, low volume procedures that are of such a complexity that it is impractical for them to exist in every large public hospital. The high regulatory burden and expertise required for islet isolation and the limitation of suitable islet donors meant that it was not cost-effective to have an isolation centre in each state and a 'hub and spoke' model similar to that developed in the UK was established. Two isolation centres, based in Melbourne and Sydney were established along with 3 transplanting centres in Adelaide, Melbourne and Sydney. Clinical efficacy was confirmed by the Australian multicentre trial with the primary outcomes of prevention of hypoglycaemia, reduction in insulin requirements and HBA1c less than 7%. The primary end point was achieved in 87% of recipients[1]. Complications were largely procedure associated and there was no mortality. Although trial numbers were small, the findings were in line with overseas experience, including several multicentre studies from North America[2,3].

The current program provides a national service, an essential requirement for all NFC applications. The cost of the procedure including travel to treatment centres, islet isolation, inpatient care and immunosuppression are covered by the NFC funding. Costs may fall as cost of immunosuppression drops and with future innovation in islet isolation. Potential recipients are assessed against standard criteria by consortium participants. All patients are placed on a single national list. Donor-recipient matching, and donor pancreas allocation criteria are developed by a standing committee of the Transplantation Society of Australia and New Zealand. Currently, donor pancreases for whole pancreas transplantation take precedence over islet transplantation. However, the success of islet transplantation has meant that pancreas transplantation alone is no longer performed and whole pancreas transplantation is reserved for simultaneous and pancreas after kidney transplantation. All patients transplanted are reported to the Australian Islet and Pancreas Transplant registry[4] – a requirement for funding – as well as to the CITR. In addition to providing excellent outcomes for patients with recurrent and severe hypoglycaemia, there have been numerous ancillary benefits. First and foremost, has been the development of expertise to offer total pancreatectomy and islet autotransplantation to selected patients with recurrent pancreatitis. Most of the patients who have been offered this procedure are children with hereditary pancreatitis. The program, that is highly collaborative provides many benefits including:

- The capacity to provide a national program of relatively safe and effective treatment for patients with severe hypoglycaemia unawareness who have failed insulin therapy and intensive medical management. Prior to this program, no other treatment options were available to this group of relatively uncommon but severely affected patients.

- It has enhanced the whole-pancreas transplantation program by using pancreata that are not suitable for whole-organ transplantation and by opening new fields for research. This is consistent with national efforts to increase the number of donors and to improve the utilisation of donated organs.
- It has provided an integrated approach to beta-cell replacement, with patients being triaged by two nationally coordinated programs that now provide the most appropriate treatment for the individual patient – be it whole pancreas or islet transplantation once other treatments have failed – based on experience and the latest evidence.
- Improved blood glucose control should deliver health advantages to individuals by reducing their risk of developing end-organ complications such as kidney, cardiac, nerve and eye disease.
- Importantly, it has provided an essential technology platform for future forms of beta cell replacement therapy such as xenotransplantation and stem cell therapy. These therapies have the potential to reach a wider selection of patients with type 1 diabetes. Improvements in organ preservation and islet yield and viability may also increase the reach of islet transplantation itself.

Whilst the UK and the Australian models are not exact replicas of each other they do share a lot of common features. They both were developed using mechanisms that are designed specifically to evaluate and introduce novel, innovative procedures into the healthcare system in a controlled manner with ongoing evaluation and development and refinement. They have successfully provided a national service to patients with the greatest need and they have been a focus for collaboration and ongoing clinical research in both whole pancreas and islet transplantation. It is somewhat ironic that the stimulus for this was the initiative and advances in islet transplantation that emanated from the US, which has yet to develop a mechanism to transition it, and fund it, in clinical practice. To an outsider, the challenge seems to be how best to absorb the high costs of indemnity, regulatory burden and clinical care in a low volume procedure that is largely confined to academic healthcare centers. The importance of this extends beyond islet transplantation to other cell-based therapies that are on the horizon. These will also aspire to transition from research to a clinical delivery model.

Conflict of Interest:

The Authors declare that they have no conflict of interests.

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