Pediatric Cardiac Surgery: Ten Years Hence

William M. DeCampli, M.D., Ph.D

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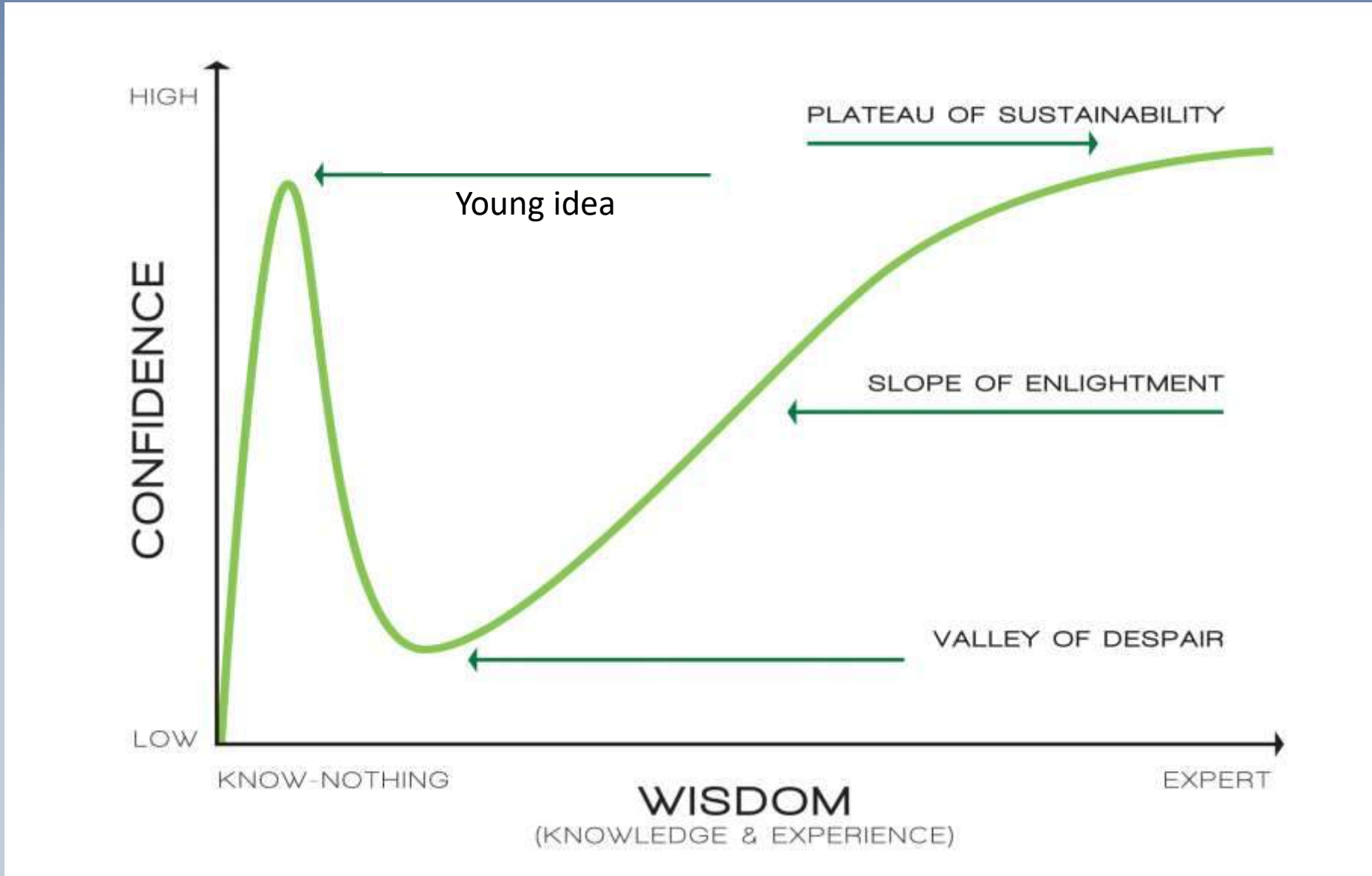
Modified Dunning-Kruger



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Pediatric Cardiac Surgical Training

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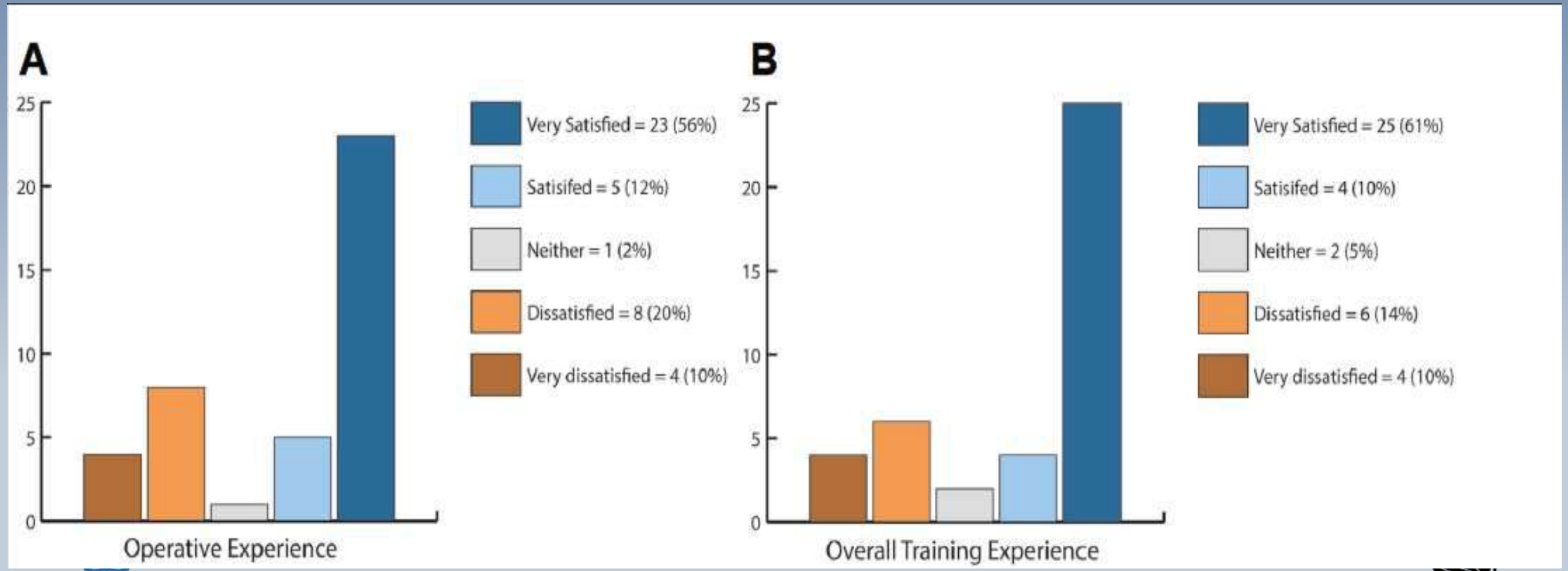
ACGME Congenital Fellowships



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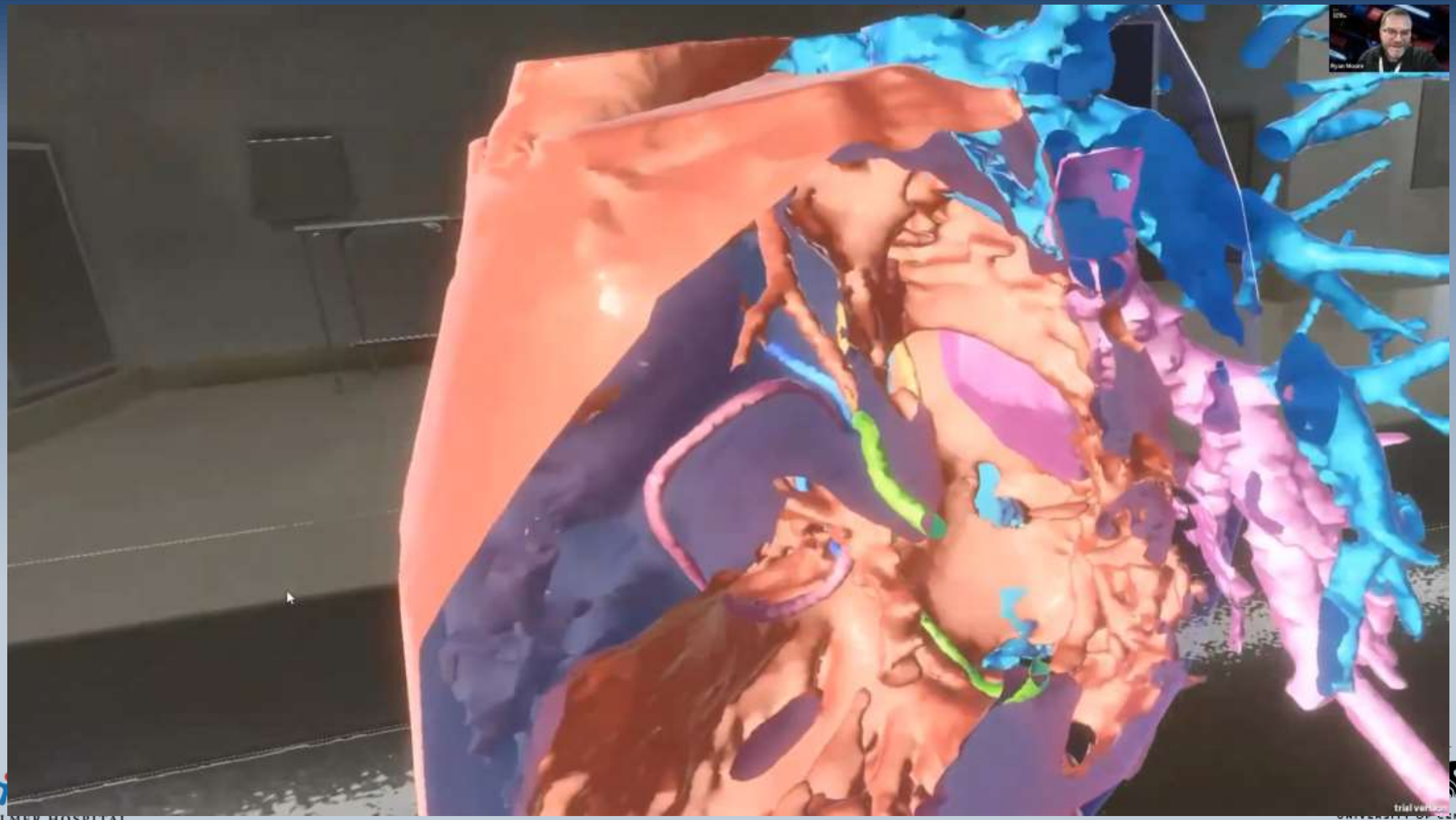

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Surgical Sam: Boston Children's Hospital

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thechamberlaingroup

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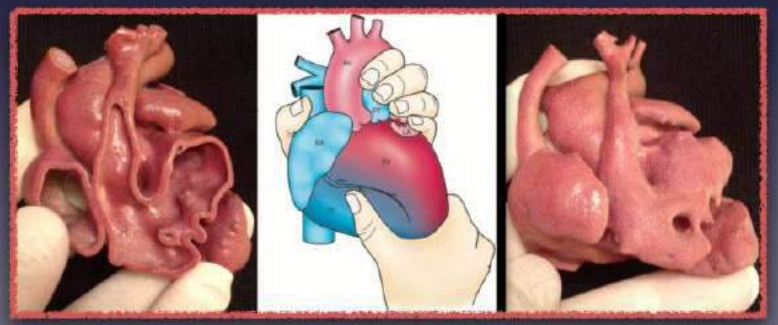
Most Peculiar Hearts in Your Hands

Criss-cross, superoinferior, twisted, topsy-turvy, etc. What do they all mean?



Shi-Joon Yoo, Omar Thabit,
Hyun Woo Goo, Whal Lee,
Deane Yim, Haruki Ide,
Glen van Arsdell

Illustrations provided by Jennifer McKinney

SickKids 3D Print Heart

DOUBLE OUTLET RIGHT VENTRICLE IN YOUR HANDS

2nd Edition

Shi-Joon Yoo, Osami Honjo,
Hyun Woo Goo, Whal Lee,
Glen S. van Arsdell

SickKids 3D Print Heart

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“Partial Heart Transplantation”

Evidence-based surgical hypothesis: Partial heart transplantation can deliver growing valve implants for congenital cardiac surgery

Taufiek Konrad Rajab

Surgery 2021 Apr;169(4):983-985.

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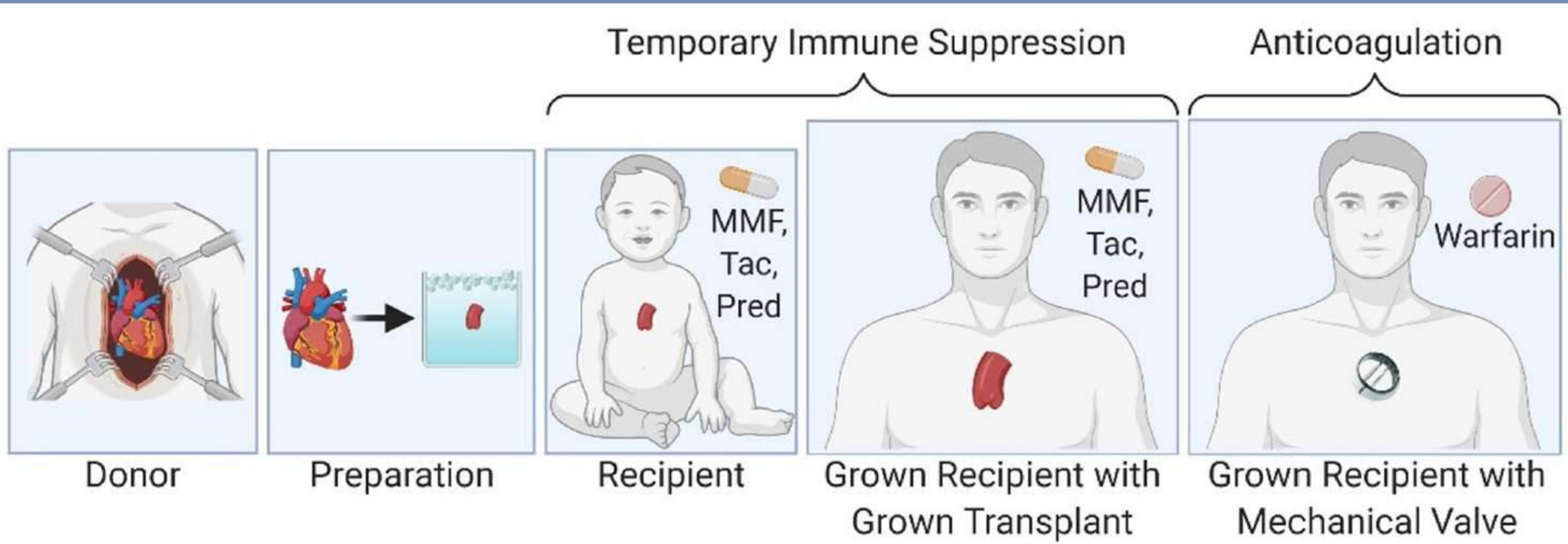
Partial Heart Transplantation



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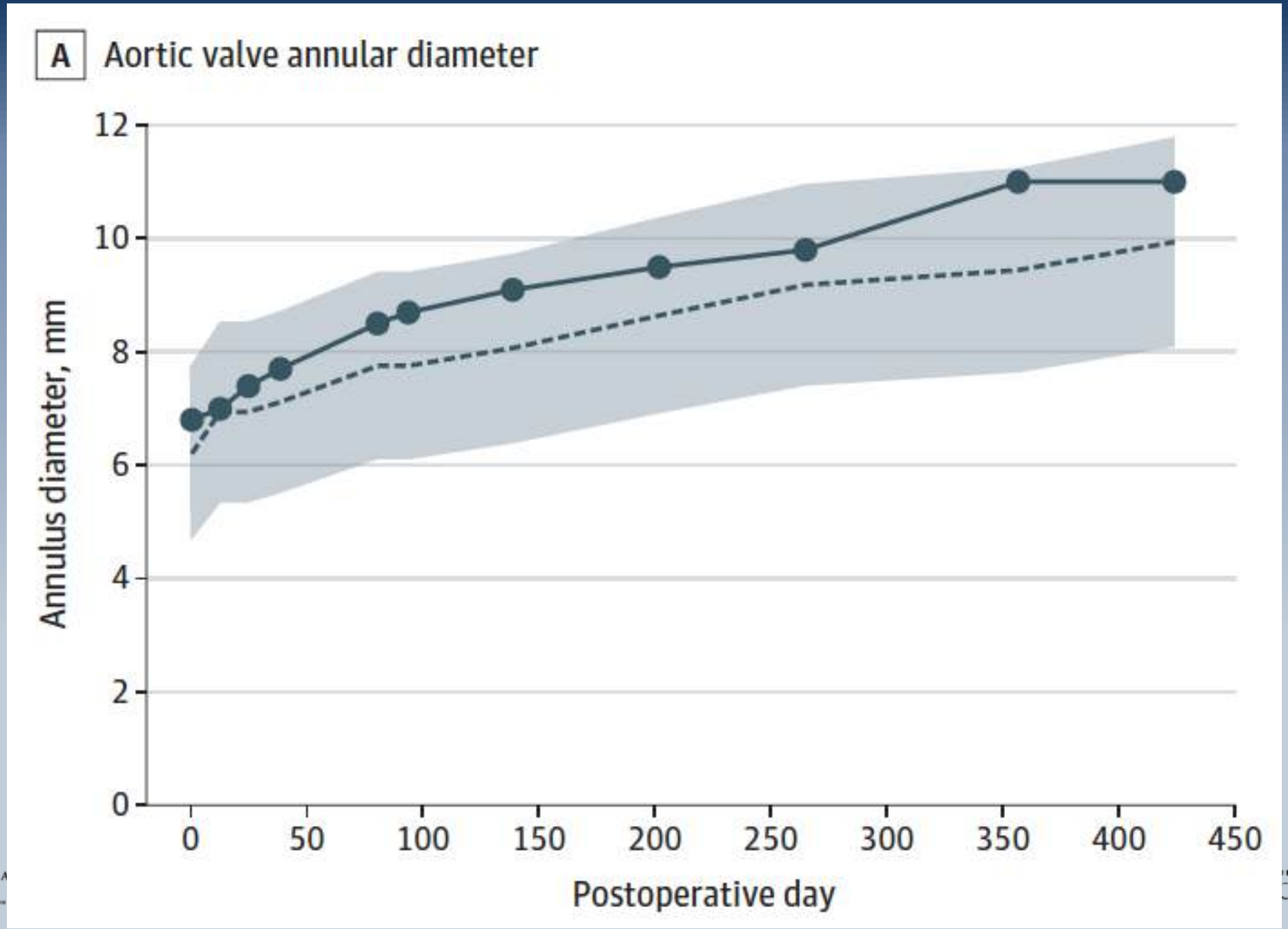

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Artificial Organs WILEY

RESEARCH PROTOCOL

Partial heart xenotransplantation: A research protocol in non-human primates

Taufiek Konrad Rajab[1] | Corbin E. Goerlich[2] | Joseph M. Forbess[2] | Bartley P. Griffith[2] | Muhammad M. Mohiuddin[2]

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Whole Heart Xenotransplantation

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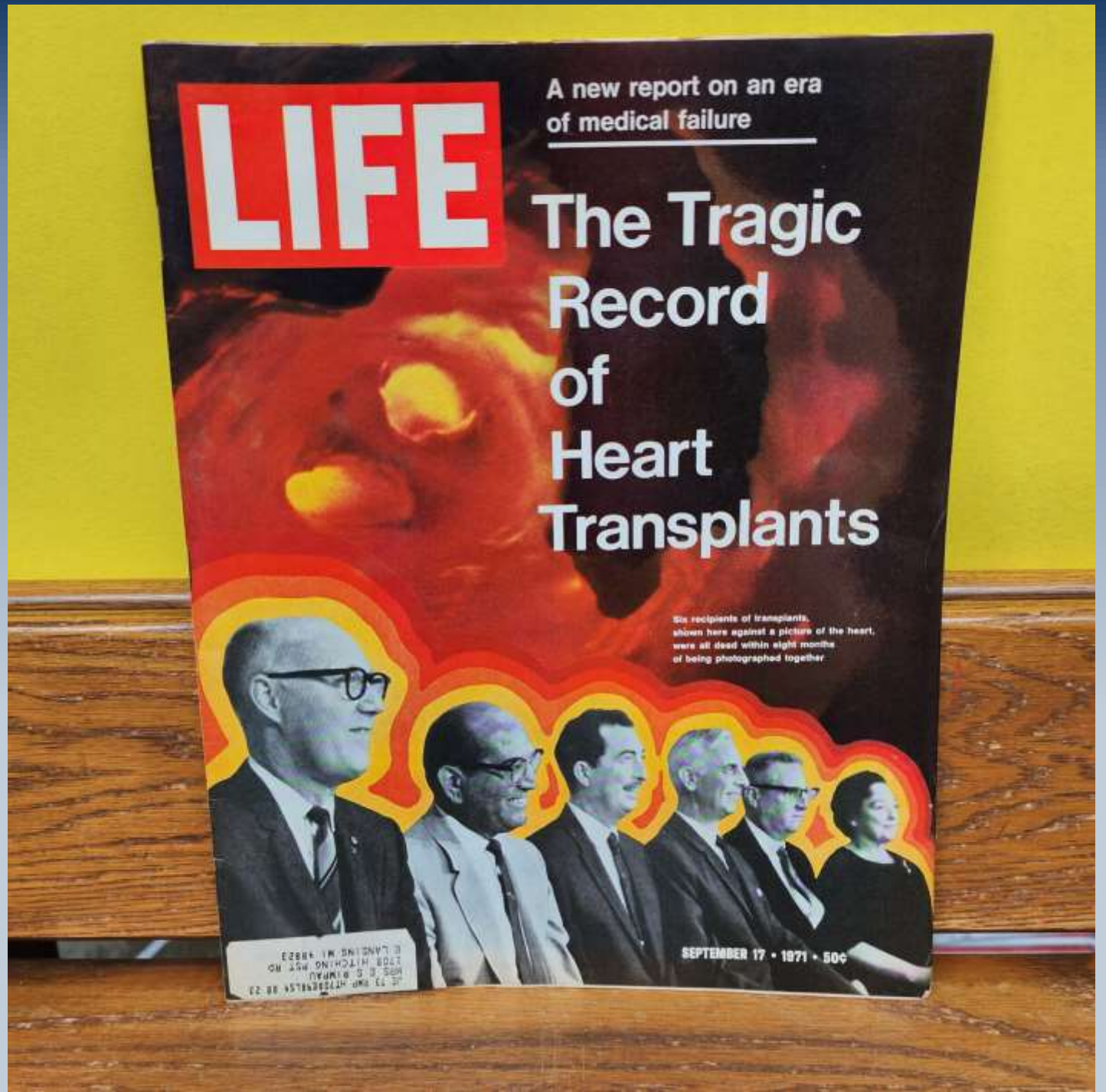
Brief History of Cardiac Xenotransplantation

Surgeon	Year	Location	Donor	Survival
Hardy	1964	Jackson, MS	Chimp	2 hours
Cooley	1968	Austin, TX	Sheep	10 min
Marion	1969	Lyon, Fr	Chimp	“quickly”
Barnard	1977	Cape Town, SA	Chimp	4 days
Bailey	1984	Loma Linda, CA	Baboon	20 days
Religa	1992	Sosnowiec, Pol	Pig	23 hours



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“Immunosuppression alone will not suffice”

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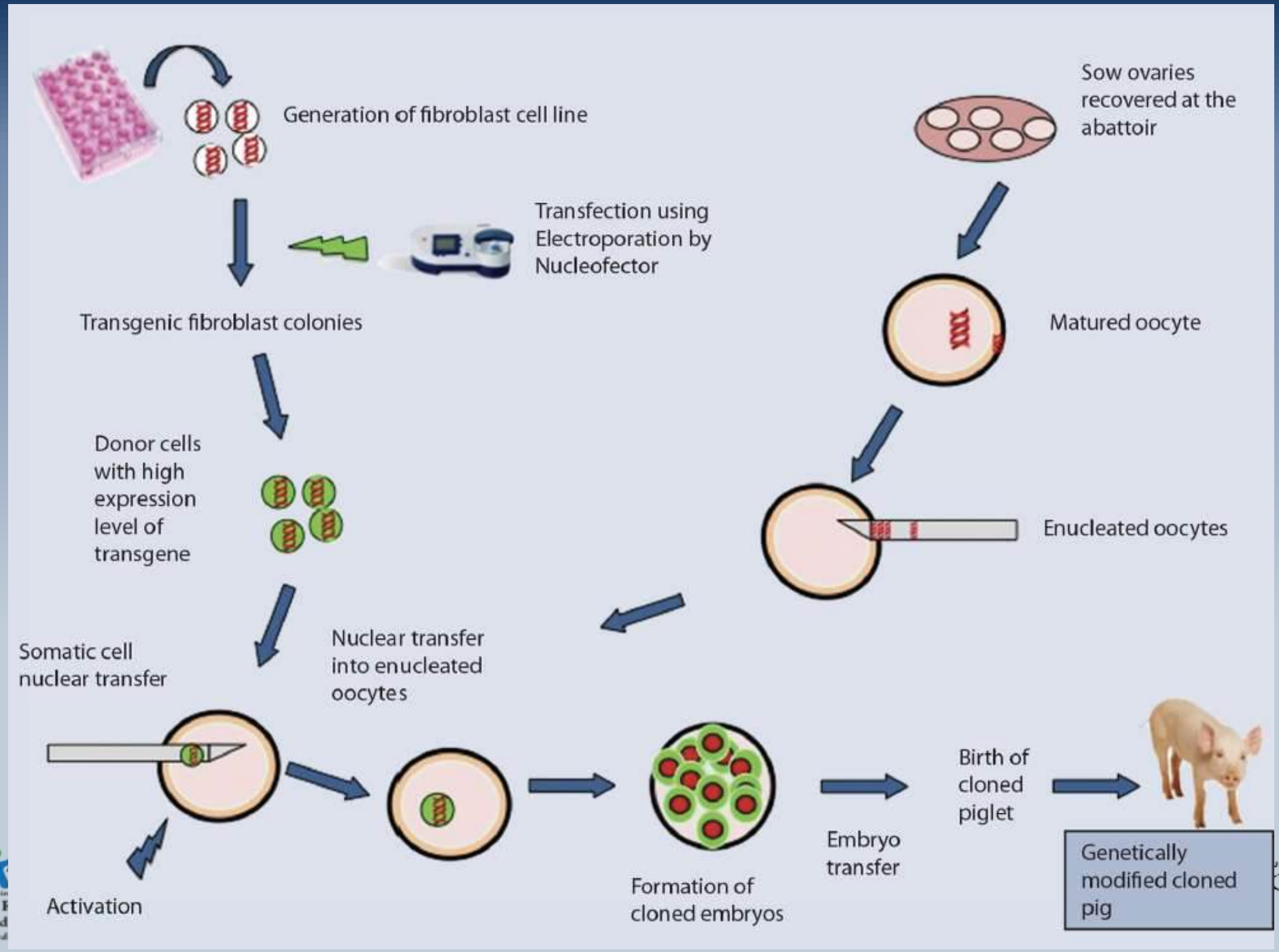
Generation of fibroblast cell line
Transfection using Electroporation by Nucleofector
Transgenic fibroblast colonies
Donor cells with high expression level of transgene
Somatic cell nuclear transfer
Activation
Nuclear transfer into enucleated oocytes
Formation of cloned embryos
Embryo transfer
Birth of cloned piglet
Genetically modified cloned pig
Sow ovaries recovered at the abattoir
Matured oocyte
Enucleated oocytes

Pig-to-human heart transplant slated to begin in 1996

The world's first xenotransplants of transgenic human–pig hearts into human recipients may be performed at the Papworth Hospital in Cambridgeshire, UK, early next year. This follows the announcement that Imutran Ltd, in Cambridge, has made significant headway in overcoming the problem of hyperacute rejection, a major hurdle in the use of animal organs for human transplantation.

At a meeting at the Royal Society of Medicine in London in September, David White, research director of Imutran, said that in the company's latest trials two out of ten monkeys were still alive more than 60 days after receiving pig hearts. The median survival was 40 days, whereas control (non-transgenic) pig hearts lasted 55 minutes. This contrasts with a maximum survival of 30 hours recorded using a similar approach by K.R. McCurry *et al.* in the United States (see *Nature Medicine* 1, 423–427; 1995).

The technique involves transferring genes for human complement inhibitor proteins into a pig fetus and inducing the pig to express the proteins, thereby tricking the human immune system into seeing the pig organ as human.

Each monkey received levels of immunosuppressants similar to those given human transplant recipients. Examination of two monkeys on days 34 and 35 with the pig hearts still beating showed them to be normal, with no signs of rejection.

Approvals for the trial will now be sought from the ethics committee at the hospital. It is expected that five or six people will receive pig hearts in the initial trial. Likely candidates will include people with rare tissue types for whom there is little chance of a suitable human donor.

John Wallwork, director of cardiac transplantation at Papworth, and a non-executive director of Imutran, said, "This research is now well advanced and we are making excellent progress in developing animal organs for transplantation — but it is important to understand that it will be several years before they are offered routinely as an alternative."

In the UK there are almost 6,000 people currently on the waiting list for a donor heart; in the USA 30,000. Fewer than half are likely to receive a heart transplant.

NUALA MORAN
London

nature medicine

Article

https://doi.org/10.1038/s41591-024-03429-1

Transplantation of a genetically modified porcine heart into a live human

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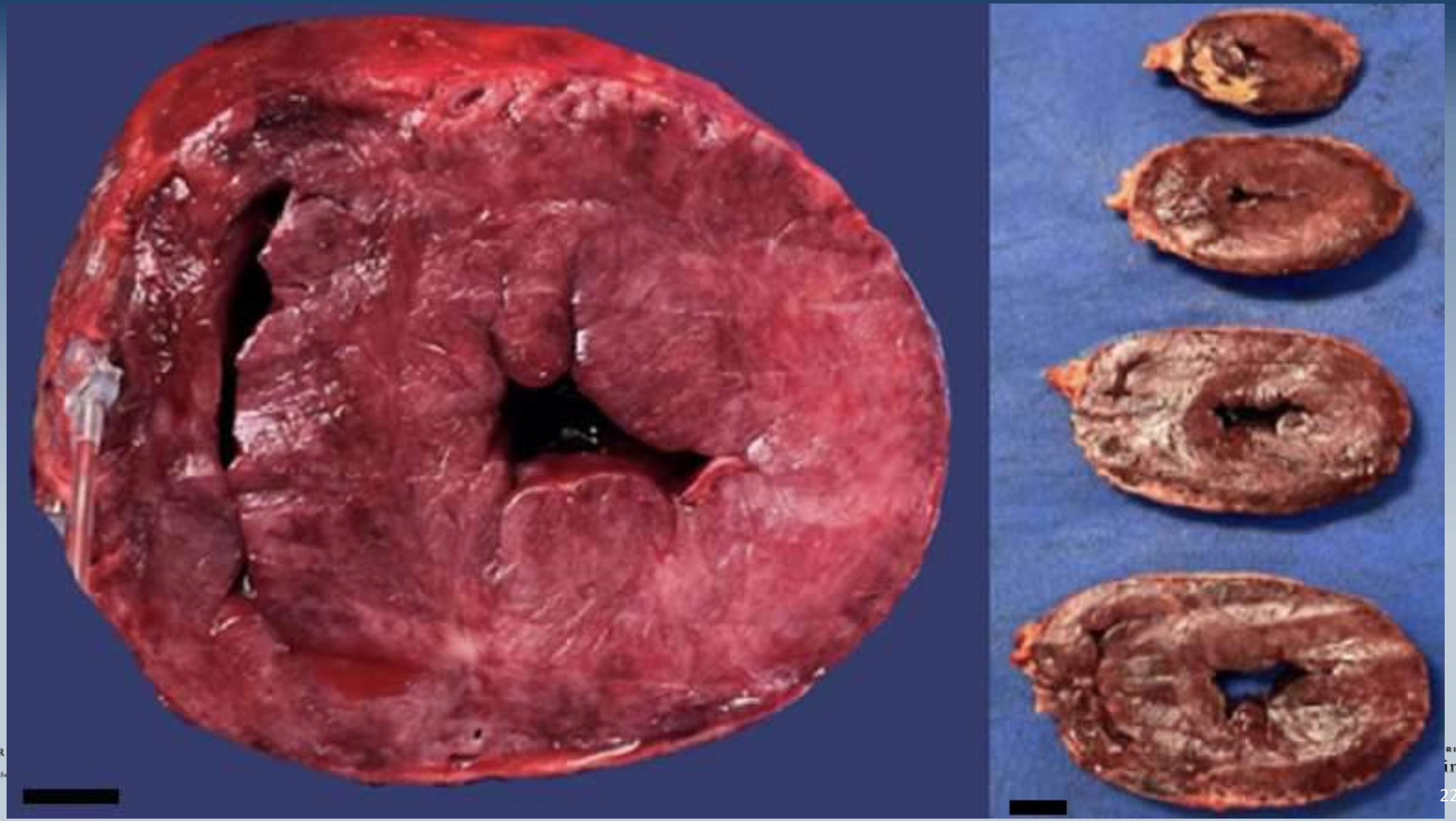

Future developments: beyond the 10 Gene Edits

- Gene knock out of SLA class I antigens (swine leukocyte antigens; analogues of HLA)
- Transgenic expression of programmed death-ligand ! (PD-L1)
- Graft cytotoxic lymphocyte-associated molecule-4 ligand production
- Knock out PERVs (porcine endogenous retroviruses)
- Eliminate need for exogenous immunosupression

Current Transplantation Reports (2025) 12:1
https://doi.org/10.1007/s40472-024-00457-1

REVIEW

Clinical Heart Xenotransplantation: A Beat or Two Away?

Imad Aljabban[1] · Jacqueline Kim[1] · Ian Jaffe[1] · Karen Khalil[1] · Robert A. Montgomery[1] · Adam Griesemer[1] · Guerard W. Byrn[2] · Alex Reyentovich[4] · Nader Moazami[5]

Accepted: 22 October 2024

Xenotransplantation Is the Future of Pediatric Cardiac Surgery

INVITED COMMENTARY:

Norman Shumway coined the aphorism that "xenotransplantation is the future of transplantation, and always will be." In this issue of *The Annals of Thoracic Surgery*, Cleveland and colleagues[1] from the University of Alabama give us a glimpse of this future. Nonhuman waitlist, the results achieved so far are clinically highly relevant.[3] Norman Shumway may soon be proven wrong because cardiac xenotransplantation may be within clinical reach.[5]

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