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LAKE COMO SCHOOL OF ADVANCED STUDIES

Lake Como School of Advanced Studies
School on Organ Transplantation June 27 – July 1, 2016
Transplantation: Complexity vs. Chaos?

Directors:
Paolo Antonio Grossi, Università degli Studi dell'Insubria, Varese, Italy
Jay Alan Fishman, Harvard Medical School, Boston, USA

Introduction:
The clinical team that carried out that first identical-twin transplantation in 1954 in Boston could not have anticipated the tremendous advances that have occurred in transplantation. Today, transplant clinicians have an armamentarium of immunosuppressive agents at their disposal, all of which are used in various combinations both for induction and maintenance immunosuppression. Loss of organs due to acute, irreversible rejection is now uncommon, and one-year graft-survival rates of 80 to 90 percent are the norm for all types of organ transplantation. Many problems remain to be solved — for example, the insidious loss of grafts from chronic allograft failure; complications associated with immunosuppressive drugs, Including nephrotoxicity, hypertension, hyperlipidemia, and diabetes; and with long-term immunosuppression, the increased incidence of infection and cancer. Furthermore, the gap between the number of organs available and the demand for organs increases every year, giving rise to serious ethical dilemmas of equity versus utility in the allocation of this increasingly valuable resource. These factors enter into the routine decisions that guide organ allocation and the care of critically ill patients.

Clinical transplantation is considered one of the medical miracles of the 20th century and remains an enormously exciting field. New scientific and ethical challenges emerge from areas such as xenotransplantation and use of organs from donors carrying HIV and HCV infection. However, such challenges and exciting scientific insights combine to make the field a dynamic work-in-progress. Some of the major achievements and disputes in this multidisciplinary clinical field will be the subject of this school which fits within the central theme of complexity.

Chaos vs. Complexity?

Decision-making in transplantation must account for numerous, individual biological factors – for which formal measurements may not exist. Physicians say the patient "looks sick." Pathologists opine "This is a good organ." These "expert" opinions are used to predict the outcomes of transplantation.

Chaos theory concerns deterministic systems whose behavior should be predictable based on initial conditions. Chaotic systems are predictable for a while and then 'appear' to become random. All donors and recipients of transplanted organs, organs, allocation systems and medical care vary greatly. These differences in initial conditions (even those which are small) produce widely diverging outcomes for such systems, rendering long-term prediction or generalization impossible. Complexity, in contrast, is generally used to characterize a process with many parts where those parts interact with each other in multiple ways. The study of these complex linkages at various scales is the main goal of complex systems theory – and the exciting subject of this course.
What is the path forward for clinical transplantation? Can the outcomes of transplantation be predicted based on the initial conditions of donor, organs, and recipients? Or are outcomes dependent on unknown or unpredictable features, and completely unpredictable?

According to theory, predictions regarding the outcomes of transplantation should depend on three factors:

- How accurately can we measure its current state? (How much do we know about what we are doing?)
- How much uncertainty can we tolerate in the forecast (how well will our patients do?)
- Over what time is stability or predictability expected? (Why do some patients fall off the curve?)

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UNIVERSITÀ DEGLI STUDI DI MILANO

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Transplantation: Complexity vs. Chaos?
Schedule

Monday June 27	Tuesday June 28	Wednesday June 29	Thursday June 30	Friday July 1
Basics of Transplantation: History, Organ Procurement and Allocation	Basics of Transplantation: Immunology and Graft Rejection	Basics of Transplantation: Clinical Challenges I	Basics of Transplantation: Clinical Challenges II	Transplantation: Complexity
9.00-9.30 Welcome and Introduction to the school: Paolo Grossi & Jay Fishman	9.00-9.40 Immunology of Graft Rejection (overview): Emanuele Cozzi	9.00-10.00 Special lecture: History and evolution of organ transplantation: Luigi Rainiero Fassati	9.00-9:40 Special lecture: Patient experience: Ernesto Dellarocca (OLTX for HCC HCV related; recent successful treatment with DAA)	9.00-9,40 Vigilance & Surveillance: Deirdre Fehily
9.30—10.10 Special lecture: Complexity and Chaos: Giulio Casati	10.00-10.40 Basics of Immunosuppression and Drug toxicity: Claudio Ponticelli	10.00-10.30 Liver transplantation – technical challenges: John Fung	9:40-10:20 Donor screening and Donor-Derived Infections: Paolo Grossi	10.00-10.40 Cultural sensitivity and education: Alessandra Grossi
10.10-10:50 The principles of gift law and the regulation of organ donation: Alexandra Glazier		10:30-11:00 Kidney transplantation – technical challenges: Franco Citterio	10:20-11:00 PTLD and malignancies in transplantation: Michael Nalesnik (Pittsburgh)	10:40-11:20 Informed consent – patient perspective Mario Picozzi
10:50-11.20 Coffee break	11.00-11.30 Coffee break	11.00-11.30 Coffee break	11:00-11:30 Coffee break	11.20-11.50 Coffee break
11:20-12:00 Presumed consent: Jacinto Sanchez Ibanez	11.30-12.10 Pathology of Graft Rejection: Antonietta D'Errico	11:30-12:00 Small Bowel and Multivisceral Transplantation: Kareem Abu-Elmagd	11.30-12:10 Post-Transplant Infections and the Microbiome: Jay Fishman	11.50-12.30 Case 4: How do we analyze complex systems? What can be fixed?
12.00-12.40 Organ procurement: Alessandro Nanni Costa		12.00-12.40 Heart and Lung Transplants – technical considerations: Mauro Rinaldi		
12:40-14.00 Lunch	12.30-14.00 Lunch	12:40-14.00 Lunch	12.10-14.00 Lunch	12.30-14.00 Lunch
14:00-14:40 Ethics in transplantation: Francis Delmonico	14.00-14.40 Cardiovascular and Metabolic complications: Anna Casu	14.00-14:30 Continuous Flow Left Ventricular Assist Devices as a bridge or destination therapy for end stage heart disease: Michele Pilato	14.00-14.40 HCV infection in solid organ transplant candidates and recipients: Patrizia Burra	14.00-14.30 Closing remarks Paolo Grossi & Jay Fishman

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14:40-15.20 Organ preservation, repair, and transportation TBD: (Sergio Vesconi)	15.00-15.40 Chimerism: TBD	14:30-15:00 Machine perfusion of the liver: past, present and future: Michele Colledan 15:00-15:30 Lung transplantation with donation after circulatory determination of death donors and the impact of ex vivo lung perfusion: Franco Valenza (Milano)	14:40-15.20 Solid organ transplantation in HIV-infected individuals: Peter Stock	
15:20-15:50 Coffee break	15:40-16.10 Coffee break	15:30-16:00 Coffee Break	15:20-15:50 Coffee Break	
15:50 – 17:00 Case 1: Allocation case (Glazier and Nanni Costa) – which individuals are worthy of organ transplants? Equal access vs. Social worthiness (excludes smokers and alcohol users) vs. maximum benefit?	16.10-17.10 Case 2: Organ Trafficking – Should this be criminalized? Francis Delmonico	Free Afternoon or Case 3?	15.00-16.30 Case 3: Xenotransplantation: Ethics (Cozzi and Fishman) – propose a case which is discussed in small groups (who get different aspects to discuss over wine) and report back to whole group	
Reception: Drinks				

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