

# **Annual report**

Transplant Centre University Hospital Zürich

2009

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## 1. The Transplant Centre in its second year - Achievements and goals

Thomas Fehr, coordinator

The 3rd International Symposium on Transplant Medicine marks at the same time the end of the 2<sup>nd</sup> year since the foundation of the transplant centre. Within this period the centre has become a central mandatory element in the structure of the University Hospital allowing to approach and to solve comprehensive discipline- and function-spanning questions and problems. The board of directors as the central operative organ with representatives of all departments and functions has proved itself a confidence-building organ capable of acting and approaching the urgent problems in its monthly meetings.

### 1.1. Achievements

The beginning of the year was marked by the *inspection of Swissmedic*, which was conducted for the first time within the scope of the new transplantation law and on behalf of the Federal Office of Public Health (FOPH). In intensive preparation under the guidance of Uschi Schäfer, data manager of the Transplant Centre, the basic process and quality documents have been recreated or adapted so that our centre passed this inspection with a good qualification. The inspection has, however, clearly demonstrated that a centre of this size and complexity is in need of its own quality management system with adequate resources in terms of personnel and material (IT!). In collaboration with Andreas Käser, clinical manager of the TPL centre, respective proposals and projects are in preparation or yet in elaboration. In May the *Swiss Transplant Cohort Study* could celebrate its one-year existence. The Zurich Transplant Centre as the largest centre in Switzerland has been able to recruit the majority of patients taking part in this study, with an acceptance rate around 95%. This success has been acknowledged in a special information even

in September 2009. PD Dr. Nicolas Müller, member of our board of directors, has been elected president of the scientific committee of the cohort.

The 2<sup>nd</sup> year has also brought about several *staff changes* in the Transplant Centre: PD Dr. Markus Weber (Division of Visceral and Transplantation Surgery), initiator, project leader and first coordinator of the centre, has left the University Hospital Zurich in spring 2008 and Prof. Thomas Fehr (Division of Nephrology) has been elected his successor. Furthermore Dr. Sarosh Irani as representative of lung transplantation has quit and has been replaced interim by Prof. Annette Boehler. Eventually Dr. Sebastian Riethmüller, clinical senior physician of the interdisciplinary transplant ward, has been replaced by Dr. Alf Corsenca after two years of committed activity.

The problem of organ shortage has aggravated in our country during the year 2009. In 2008, 62 patients from the waiting list have died in Switzerland compared to 459 performed transplantations. In the University Hospital Zurich the number of multi-organ donors has again been regressive in 2009. At the same time, however, the number of donors within the scope of the hospital network supervised by the USZ could be further increased. The Transplant Centre is aware of the urgency of this problem. Under the guidance of Prof. Reto Stocker, member of our board of directors, a well attended public symposium on the subject of organ donation has taken place in early summer 2009 at the USZ. In the fall 2009 two working groups have been formed in the Transplant Centre who will specifically dedicate themselves to this subject.

### 1.2. Goals

In the year 2010 our Centre will have to face a number of challenges. As mentioned before, *measures for the promotion of organ donation* are in the focus. On the one hand, this aim may be reached by intensified PR work in close collaboration with the communication department of the USZ. On the other hand, in-house hospital measures should also be taken.

From a medical point of view, living organ donation must be further advanced, in the case of the kidney by upgrading the programme for ABO-incompatible donation as well as by the implementation of a desensitization programme. As far as cadaver donation is concerned, the re-launch of transplantation of so-called "Non heart-beating donors" (NHBD) is planned in the scope of a nationwide project. In Switzerland, the USZ has held a cutting edge for years in the renal transplantation of NHBD. The

resumption of the programme for renal and liver transplantation will present the centre with considerable coordinative and logistic challenges, which we are willing to tackle.

In the year 2010 the USZ as our basis will be completely re-organized and divided into 9 medical and service domains. The various clinical divisions involved in transplantation will be assigned to completely different domains, and therefore the coordinative tasks for the centre will increase. The precise position of the transplant centre within the new hospital organization has not been defined so far ad will be the subject of negotiations in the year 2010. This regards in particular the interdisciplinary organs of the transplant centre, namely transplantation coordination, the interdisciplinary HLA typing laboratory as well as the organs of the cohort study and the quality control.

The 2nd birthday of the transplant centre has been celebrated with the 3<sup>rd</sup> International Symposium of Transplantation Medicine, and we are proud that so many top-class speakers have accepted to join us in Zurich for this event. The symposium was dedicated to the topics "Transplantation in the elderly patient" and "Transplantation of NHBD" and thus touched two burning subjects of transplantation medicine, which will keep our centre busy in 2010 and which we are going to approach with verve!

## 2. Centre-specific and integrative services

## 2.1. Transplantation coordination

Werner Naumer

As a consequence of the implementation of the new transplantation law in July 2007, we are in the meantime supervising 23 network hospitals with intensive care units. This means among other things that we provide further training in these hospitals with the objective to instruct and advance the staff. In order to avoid that the organ donors have to be relocated in certain hospitals, the coordinators go onsite in order to coordinate the donation and harvest the organ. From a logistic point of view, this is very challenging and requires a lot of experience and routine. The workload has increased recently. In case of the presence of several organ donors at the same time, 2-3 coordinators may be required also for security reasons in order to manage the workload.

The collaboration with the cantonal and extra-cantonal hospitals is excellent.

Our hotline for potential organ donors has become well-established and is frequently used.

The total number of services (including "foreign offers") provided by the transplantation coordinators per year lies between 220 and 240, which corresponds to a total of >1500 working hours.

Due to the increased presence of the Federal Office of Public Health in the media, the interest of the population for the subject has become more vivid. It is also our task, in addition to providing instruction in nurse's training schools, to go to local associations in order to make people more familiar with the subject of organ transplantation. We are pleased to provide information by presenting on-site lectures. Often uncertainties and fears can be dissipated that way.

## 2.2. Interdisciplinary HLA typing laboratory

Barbare Rüsi

The HLA typing laboratory is an interdisciplinary laboratory under the supervision of the Division of Visceral and Transplantation Surgery. Since 2009 the medical direction of the lab consists of Prof. Dr. Thomas Fehr (chief physician, Division of Nephrology), PD Dr. Markus Müller (chief physician, Division of Visceral and Transplantation Surgery), and Dr. Georg Stüssi (senior physician, Division of Haematology).

While no remarkable innovations have resulted in the recent years for the methods of HLA typing and the application of crossmatch testing, the typing of the anti HLA-antibodies appeared in a completely new light thanks to the implementation of flow cytometry with Luminex. By means of the sensitive Luminex technology it became possible to specify the anti HLA-antibodies in the serum of the patient for HLA-class I as well as for HLA-class II. So far it has in fact been possible — on a very low sensitivity level — to identify antibodies for HLA-class I. A specification of the HLA-class II antibodies, though, could only be obtained

with the implementation of the Luminex technology. Since January 2008 all sera of patients are routinely quantified with this method upon admission to the waiting list and once yearly thereafter and are also specified in case of positivity.

In a study performed retrospectively in collaboration with the Swiss reference laboratory in Geneva (Dr. S. Riethmüller, Prof. Th. Fehr, PD Dr. J. Villard) the importance of these highly sensitive tests with regard to rejection rate and transplant function in the first year following renal transplantation could be confirmed.

After the personnel of the interdisciplinary HLA-typing laboratory had been increased in the course of the last year, preparations for the accreditation could be started this year. The objective of the interdisciplinary HLA-typing laboratory is the specialty accreditation according to the EFI (European Federation of Immunogenetics) by mid-2010.

## 2.3. Research in the Transplant Centre

Rolf Graf

In addition to the established basic and clinical research in the Transplant Centre yet another question has arisen in connection with the new transplantation law and the rules of allocation. As a consequence of these new rules, the organs are allocated centrally, irrespective of the place of the organ donor. Thus patients who are very sick and have been on the waiting list for a long time are considered with priority. With the strongly increasing morbidity of the recipient complication rates increase as well and thus morbidity and mortality. This new situation is currently being evaluated in clinical studies in order to implement potential improvements in the patients' management..

Besides the current studies contributions on various subjects have been published. Central issues have been approached, e.g. on the effect of long-term intake of immunosuppressors on different organs, especially on the skin and the lung, which are particularly at risk because of their exposition. The question, what effects the infection of donors' organs with aspergillus can have on the recipients was also discussed.

Furthermore efforts have been made in xenotransplantation towards a better understanding of the rejection reaction. The optimization of the perioperative treatment for improvement of the outcome following liver surgery was also subject of investigations. The publications of the current year are summarized in the attachment.

## 2.4. Continuing education

Nicolas Müller

The objective of the monthly seminar of the Transplant Centre, "Hot Topics in Transplantation" with national and international experts is to make organ-spanning subjects of general interest accessible to a broader audience. The financing is guaranteed by generous "unrestricted grants" of all relevant companies interested in transplantation. This year, too, an exciting programme with contributions from different areas was put together. In particular the lecture by Dr. Franz Immer, Director of Swisstransplant, on the experience with the new allocation system, was met with great interest.

## 2.5. Swiss Transplant Cohort Study (STCS)

Nicolas Müller

Since the start of the recruitment for the Swiss Transplant Cohort Study on May 1<sup>st</sup>, 2008, more than 200 patients have been included in Zurich. Since October 1<sup>st</sup>, 2009, stem cell transplanted patients are also admitted. All Swiss centres with transplantation activity take part in this ambitious project. Thanks to the enormous support of all participants everything proceeded smoothly. The first scientific studies have been started after evaluation by the Scientific Committee.

## 3. Patient care in the transplant centre

## 3.1. Mentoring of organ donors

Reto Stocker

So far, the year 2009 has been characterized on the one hand by the fact that we had only two organ donors at the USZ until November, one of whom was eventually found unsuitable for organ donation, and on the other hand by a very important activity in the Zurich network, from where totally 11 organ donors were allocated. Since the contracts with the network hospitals will expire by the end of 2009, we are currently collaborating with the legal department of the USZ and the Ministry of Health of the Canton of Zurich in view of a continuation. As the donor situation at the USZ demonstrates, this is of utmost importance, since the creation of a network has led to increased allocations of organ donors.

The fact of the decreasing number of organ donors at the USZ has been noticed with great concern not only by us, but also by the Comité National du Don d'Organes CNDO (International Committee of Organ Donation) of Swisstransplant. This committee has been funded with the support of the Health Directors Conference (GDK) in 2008 with the intention to promote organ and tissue donation in Switzerland and to coordinate the respective training and PR efforts nationwide.

With the support of the intensive care physicians in the USZ an external audit has been conducted at the USZ on August 19, 2008 in order to analyze the donor situation at the USZ on the occasion of a meeting between Prof. S. March (Cantonal Hospital Basel), Prof. R. Stocker (Head, Division of Surgical Intensive Care Medicine USZ) and members of the USZ transplant coordination (Mrs T. Reh, Mrs F. Walther and Mr W. Naumer). The report based on the visit and the ensuing detailed assessment of the documents provided has been discussed in the CNDO.

### **Summary of report**

If the number of donors per calendar year is < 3, as in the present situation, a statistically significant difference compared to previous years has to be assumed. When extrapolating the numbers of national donors, approximately 1 organ donor per 100 000 inhabitants can be expected in our country. The USZ as centre for the large urban agglomeration of Zurich (about 2.5 Mio inhabitants) would accordingly have to contribute a total of approx. 25 donors (in-house and allocated). In fact, however, the average total number of donors at the USZ over the recent years was 11 (95% confidence interval 7-15), whereby in 2009 the USZ-internal recruitment of organ donors is significantly below the long-standing own average of 8 donors per year and also significantly below the 95% confidence interval of 3 donors per year. Thus the low donor rates appear to be not just a matter of difference within the statistical range.

### In its analysis the report arrived at the following conclusions:

- The USZ disposes of a long-standing systematic data monitoring of death cases in intensive care units with external control. The existing data are reliable and credible. There are no indications that organ donors would not be detected as such in the intensive care units of the USZ. It is, however, striking that the period until withdrawal of treatment sometimes appears rather short and consequently also the observation interval for detection of neurological aggravation and progression toward brain death can be quite tight.
  - It has to be admitted, though, that also in case of a longer observation interval hypothetically only 0 2 organ donors at maximum would have been recruitable. Considering the high degree of bed capacity utilisation, considerable pressure from the bed capacity has to be assumed. Therefore, the reason for the low donor rates is not insufficient donor detection in the intensive care units, as is claimed by certain transplant surgeons.
- In patients with signs of brain death, the refusal rate of 20% (7 out of 35) by relatives and patients themselves is not strikingly high. There are significant differences between the intensive care units of the USZ with regard to refusal rate for organ donation. These differences are not new, but exist since several years and therefore do not explain the current low donor rates.

Altogether there is no obvious cause for the low organ donation rate at the USZ. Potential donors are not "overlooked" in the intensive care units.

### For the above reasons, we are confronted with the following questions:

- a. Is there at all a sufficient number of patients entering the USZ with a diagnosis that could potentially lead to brain death?
  - i. If not, why has this no longer been the case recently?
- b. Is there at all a sufficient number of patients entering an intensive care unit of the USZ with a diagnosis that could potentially lead to brain death?
  - i. If not, why has this no longer been the case recently?
  - ii. If so, why do these patients no longer reach the state of brain death recently?

### **Further procedure**

According to the CNDO the USZ the responsible persons at the USZ can be advised as follows: There is no obvious and/or problem with a simple solution in the *intensive care units* of the USZ. Thus the question arises whether there could be a complex problem in the *USZ system*. Therefore the CNDO is recommending a survey of diagnosis-relevant outcome data. To this end all patients with the diagnoses stroke, brain haemorrhage, craniocerebral trauma and status after resuscitation would have to be systematically recorded and tracked upon entering the USZ. Like this it would become transparent whether there is at all a "critical mass" of potential organ donors available, and if so, where potential organ donors "disappear" in the USZ.

This should allow for rational steps toward process optimization. Of course such a data survey is connected with considerable expense and effort, requires corresponding personnel resources and is beyond the means of the CNDO. However, the CNDO is of course willing to assist us with the planning of the survey and to act as advisor in the evaluation and interpretation of the acquired data.

- The exemplary and complete documentation of all death cases in the intensive care units has to be continued unchanged.
- The active participation in the projected national donor study (scheduled start 2010) has already been initiated.
- Clarification of procedures in case of treatment withdrawal in intensive care patients with neurological symptoms. A checklist considering the concerns of organ donation is currently being compiled by the IT and will be implemented as new form for death cases in the beginning of 2010.
- Analysis of the variable refusal rate of organ donation by relatives in the different intensive care units
  of the USZ. In this regard the CNDO has proposed an audit between a member of the CNDO and the
  responsible persons in the intensive care units of the USZ. The proposal has been welcomed by the
  respective intensive care physicians, and first steps for the audit have been initiated.
- From my point of view there is also a need for national guidelines concerning the handling of information toward relatives in case that brain death has to be awaited over a period of several days.

### 3.2. Anaesthesiologic aspects of transplantation

Marco Zalunardo

Anaesthesiology represents an essential interdisciplinary "interface" in transplantation medicine. The surgical disciplines, but also intensive care medicine, cardiology, pneumology, hepatology, nephrology, and transplantation coordination are important team partners. The interfaces or rather contact points are on the one hand preoperatively in the medical assessment, risk evaluation and patient information and in the common discussion and listing of the patient, furthermore intraoperatively in anaesthesia and securing of the vital function of the essential organ systems, and finally postoperatively in intensive medicine and pain therapy. As the number of transplanted patients is continuously increasing and the outcome and survival rate are constantly improving, surgical interventions and thus anaesthesia in already transplanted patients have become more common. All of this requires special knowledge with regard to the specific primary diseases, immune suppression and their potential influence on the anaesthesiologic management.

Transplantation medicine is a main focus of the Institute of Anaesthesiology (IFA). Since more than 15 years the IFA places several teams of specialists at permanent disposal: the anaesthesiology team for multi

organ harvesting, a team for heart transplantations, for kidney and pancreas transplantations and a separate team for lung and liver transplantations. These teams are on stand-by duty independent of each other and consist of an anaesthesiology nurse, an assistant physician, a senior physician and a specialist background service (usually a leading physician or experienced senior physician). These high specialist competence and personal commitment are unique in Switzerland.

Also in the field of research the IFA is engaged in transplantation medicine. Currently there are ongoing clinical studies on postconditioning with the anaesthetic gas Sevofluran in liver transplantation (Prof. Dr. B. Beck Schimmer) or on the influence of reperfusion on cardiac function in liver transplantations, an investigation by means of intraoperative transesophageal echocardiography (PD Dr. M. Zalunardo, PD Dr. D. Bettex). A retrospective investigation on the influence of preoperative right-ventricular function on the outcome after lung transplantation has just been concluded.

## 3.3. Hospital ward E OST III

Sebastian Riethmüller, Alf Corsenca

As far as postoperative patient care is concerned, the interdisciplinary ward is the local and organizational heart of our transplant centre. Practically all freshly transplanted patients (with the exception of heart- and bone marrow recipients) as well as the living organ donors of kidney and liver are attended to postoperatively on this ward, whereas the patients profit of a close interdisciplinary collaboration between the various medical specialties. The clinical senior physician acting on the ward plays a key role, as he is calling in the relevant specialists, stays in continuous touch with them, directly incorporates their recommendations in the patients' treatment and keeps track on each patient's history and state of health at all times. Since the beginning of September 2009, Dr. Alf Corsenca has token over this position as successor of Dr. Sebastian Riethmüller, who has changed to the Clinic of Nephrology of the USZ. Dr. Corsenca is internist and nephrologist, disposes of long-term experience in the treatment of kidney-transplanted patients and is scientifically active in this field as well.

During the reporting period, considerable emphasis was put on the further improvement of patient education. By means of the systematic oral and written information patients have to learn to "take care of their health" more consciously, in order to being able to pay more attention and react appropriately to somatic changes (e.g. changes of blood pressure, micturition, body weight and –temperature as well as nausea, vomiting and diarrhea). To this aim, a new patient brochure has been compiled predominantly by our nursing specialists, which contains among others a concept for self-monitoring of eight simple physiological parameters and states, to which the patients learn to react with a two-scale system of escalation. This programme helps to improve the collaboration between physician and patient and thus improved medication compliance and finally an improved outcome of patient and transplant can be achieved.

### 3.4. Inpatient care in the Transplant Centre

Beatrice Biotti

With the implementation of a systematic patient education following renal transplantation an interdisciplinary and interprofessional concept could be realized.

After transplantation patients have to learn to integrate a complicated medication schedule into their everyday life and to assess and interpret changes in their body.

In the concept implemented at the end of 2008/beginning of 2009 patients are prepared systematically for the hospital dismissal and a method that fits into the respective situation and environment is sought to foster patient adherence. Thus the organ survival is secured in addition to the medical measures. The active inclusion of the patients improves their independence, which has a positive effect on the success of treatment.

With regard to the SwissDRG we consider a systematic patient independence meaningful also because the length of hospitalisation does not need to be extended by purely supporting aspects of patient care. Thanks to early mobilisation of their resources patients feel faster safe with the new situation and the length of hospitalisation may be shortened as a consequence.

### 3.5. Follow-up of organ transplanted patients in dermatology

Günther Hofbauer

Recipients of solid organs and also of bone marrow/stem cells are seen in clusters in the specialized consultation for immune suppressed patients of the Clinic of Dermatology. Under the guidance of PD Dr. Günther Hofbauer more than 1'500 consultations were held in the year 2009. The main focus of this consultation is on prophylaxis, early detection and treatment of the white skin carcinoma (spinocellular skin carcinoma), which represents the most frequent malign tumour as consequence of long-term immune suppression. On the one hand existing tumours are detected and removed within the scope of the pre-transplant assessment. On the other hand transplanted patients are advised of the risk of white skin cancer and are taught prevention by appropriate behaviour, clothing, application of sunscreen and early detection.

In order to improve the long-term outcome of organ transplantations, patients attending this specialized consultation are switched to mTOR inhibitors, a probably less skin cancer causing class of immune suppressors, in the scope of the multicentric Tumorapa study coordinated by Prof. Sylvie Euvrard, Lyon. As a collaboration between the Division of Nephrology and the Clinic of Dermatology of the USZ, a basic study is dealing with the impact of azathioprine, a frequently used immune suppressor, on the photosensitivity of the skin and thus on the long-term susceptibility to white skin cancer. In this study, the medication has been switched from azathioprine to mykophenolate in 23 kidney transplanted patients, and concomitantly a significant improvement of the photosensitivity of the skin to UVA has been observed. We suppose that this will result in a significant reduction of the risk of skin cancer development.

In the year 2009 synthetic alpha-MSH has been used as internal sunscreen for the first time in Zurich as one of several centres worldwide. This study intents to demonstrate a reduction of the risk of skin cancer by increased tanning and thus increased sunscreen of the skin within two years. The recruitment will be concluded by the end of 2009.

## 4. The individual transplant programs

## 4.1. Allogeneic stem cell transplantation

**Urs Schanz** 

With 34 the number of allogeneic stem cell transplantations in the year 2009 has remained stable compared to the previous year. The number of intricate and complication-afflicted unrelated stem cell transplantations (n=15) has again increased compared to the previous year and at present constitutes almost 50% of all transplantations. Likewise the haploidentical transplantation (n=4) has been further developed. In spite of the increasing complexity of transplantations, peritransplantation mortality (day 100) is fortunately low with < 3%. As stem cell source predominantly peripheral blood stem cells are used, while bone marrow is just exceptionally used. Furthermore, Zurich is still one of 3 harvesting centres of allogeneic stem cells and has successfully continued this activity.

The close collaboration with the interdisciplinary HLA laboratory could be continued in the present year. There are common efforts to accredit the lab according to the international quality standard of the European Federation for Immunogenetics (EFI).

### 4.2. Heart transplantation

Georg Noll

The heart transplantation programme was started at the USZ in 1985.In the course of the past 24 years 354 patients have been transplanted, 8 of whom in 2009.

This extraordinary result could only be achieved through interdisciplinary patient care prior, during and after surgical intervention.

Patients with cardiac failure are attended in a special consultation of the Clinic of Cardiology and assessed with regard to heart transplantation if required. The numbers of the recent years demonstrate that the problem of cardiac insufficiency represents an increasing issue in health policy, as patient consultations have significantly increased in the course of the last years (Fig. 1). In spite of intensive attendance and optimal medicinal therapy a large part of patients is still symptomatic. Fortunately intracardial defibrillators (ICD) and instruments for resynchronisation are available nowadays, which significantly improve the patients' life quality and prognosis. These device programmes are realized in collaboration with the cardiac surgeons. In patients who are resistant to treatment an assessment is made in view of heart transplantation. In consensus with cardiologists, cardiac surgeons, cardiac anaesthesiologists and specialists of psychosomatic medicine patients are included in the list of heart transplantations.

Fig.1: Consultations in the heart transplantation ambulatory 2006 - 2009

# 2006 2007 2008 1009 HTPL EMB Total A MBI

### Consultations 2006 - 2009

In patients with heavily compromised hemodynamics assist devices are implanted as bypass to transplantation. The programme has been established some years ago and has gained increasing importance. 8 assist devices have been implanted within the last two years. The interdisciplinary attendance of these patients requires an enormous input of logistic and personnel resources. The patients are seen weekly in a special consultation by attendants specialised in cardiac insufficiency, cardiologists and cardiac surgeons as well as experts in psychosomatic medicine. Vital functions and capacity are documented at close intervals. Only in this way patients with assist devices can be transplanted successfully.

The interdisciplinary collaboration with infectiologists, cardiologists and cardiac surgeons in the early post-transplant phase has been optimized in the course of the recent years. As a consequence of the assist-device programme and intensified post-transplantation attendance the input of time and personnel resources has exceeded the reasonable limits.

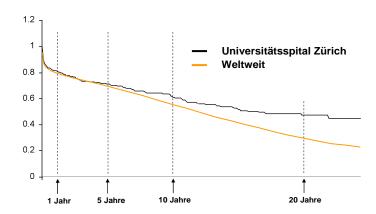
The commitment of all persons involved in the programme is reflected in the excellent long-term survival data (Fig. 2).

Fig. 2: HTPL Zurich – an international survey

- Survival rate after HTPL Zurich 1984-2008 (Kaplan-Meier)
- Worldwide survival rate after HTPL 1982-2006 (Kaplan-Meier)

### HTPL ZÜRICH - Im internationalem Vergleich

Überlebensrate nach HTPL-Zürich 1984-2008 (Kaplan-Meier) Internationale Überlebensrate nach HTPL 1982-2006 (Kaplan-Meier)



On January 30, 2009, a incore (left ventricular assist device) could be explanted fort he first time in Switzerland in a female patient after peripartal cardiomyopathy.

The productive interdisciplinary collaboration is further reflected in the large number of joint continuing education and professional training events.

Dr. Matthias Hermann, who has been working as senior physician of cardiology in the heart transplantation team, has taken over the position of chief physician in the Clinic Wald some months ago and has thus become a competent partner for the rehabilitation of heart insufficient and heart transplanted patients.

### 4.3. Lung transplantation

Annette Boehler, Sven Hillinger

In the last year, 26 lung transplantations were performed with a one year survival rate of 91%. However the new transplantation law does not prove to be useful in the setting of two lung transplanting centers in Switzerland. The central allocation is causing a change of strategy and is unsatisfying in many ways. Consequences are more complicated postoperative courses as the optimal donor recipient constellations cannot be choosen according to the current individual and local situation. This leads to a longer waiting list and much longer waiting time for certain patient groups. At the time of transplantation many are in a worse overall condition. We performed more transplantations in intubated recipients or recipients on ECMO than before. We will have to find new algorithms of priority to meet these needs.

Amongst these complicated and sometimes long term courses the team in our ICU has again done a tremendous amount of work to realize our constantly good results.

The close collaboration between the teams gets more than ever important and results in an optimal transition from ward treatment to ambulatory care in lung transplant recipients.

Regular interdisciplinary meetings between doctors, nurses, physiotherapists and other non medical professionals have been continued and have helped to establish a high standard on daily care and to solve complex problems in patient management.

Regular educational TNT seminars help to concentrate specific informations on transplantation topics on a clinical and research basis.

For the second symposium in November 2008 Prof. Dirk van Raemdonck from Leuven presented their clinical and experimental experiences about non-heart beating donors (NHBD) for lung transplantation in front of a highly interested audience, a very hot topic in times of organ donor shortage. In this sense we have applied successfully for the permission to integrate category 3 NHBD in our program and the process of optimizing the regulations therefore is about to be completed.

Internationally and nationally, members of the medical and surgical lung transplant team were very active in serving for various scientific societies as board members, scientific grant reviewers and organizers of international meetings as well as serving in lay organizations (ethical committees etc). In her new role as president-elect of the Swiss Respiratory Society, Prof. Annette Boehler, will increase awareness of lung transplantation including the impact of the new transplantation law within our medical society. Otherwise there were also changes in the team: Dr. Sarosh Irani left the medical transplant team for a position as head of Pneumology in the cantonal clinic of Aarau. Here we would like to thank him for his excellent work towards the transplanted patients. He is followed by Dr Chris Benden an experienced transplant pulmonologist and Dr. Macé Schuurmans. Within the surgical team Dr. Peter Kestenholz and Dr. Ilhan Inci also started to perform the transplant procedure in a highly professional manner. At the same time we continue our ongoing clinical and experimental research especially in applying experimental models of lung transplantation in mice, rats and pigs focusing on acute and chronic rejection as well as ischemia/reperfusion injury and ex-vivo perfusion for marginal donor lung reconditioning. Thus the year of reporting was very successful resulting in 10 original publications and several reviews from the Lung Tx program.

### 4.4. Liver transplantation

Philipp Dutkowski, Andreas Geier

In July 2007 the new transplantation law has been implemented nationwide by allocation of the donor liver according to the so-called MELD score (Model of End Stage Liver Disease), which represents a measure for the severity code of the liver cirrhosis. The amended law effects that the most severely diseased patient (highest MELD score) on the waiting list at a time receives the offer for the liver. On the basis of the amended law a decrease of mortality on the waiting list due to fair-minded and objectifiable allocation of organs was expected. The effects on the perioperative course in the University Hospital Zurich have been analyzed by now.

The number of liver transplantations at the University Hospital Zurich increases continuously (Fig. 1). A comparison between the first and last 76 patients prior and since the implementation of the amended law has revealed a significant decrease (13% vs. 25%, p=0.03) of the number of patients on the waiting list who died prior to a liver transplantation. In this respect, the amendment has a significant positive lifesaving effect. At the same time, however, there was consequentially a significant increase in the MELD scores of recipients at the time of the liver transplantation. Whereas merely one-fifth of patients showed a MELD score of more than or equal to 25 before July 2007, the percentage of seriously diseased patients with MELD of more than 25 was doubled to 41% after the implementation of the new law (Fig. 2) (p=0,0011). The median MELD score at present is at 22 vs. 15 previously (p=0.032). This increase in the severity code of liver transplanted patients has its effects on the postoperative course. Since the amendment there is a significant increase of the number of patients requiring an intermittent kidney replacement therapy (41% vs. 15%, p=0.01), whereupon the kidney function recuperates within a few months.

It has to be emphasized, however, that co-morbidities, length of stay in intensive care units, length of inpatient hospitalization as well as survival rates (1-year survival rate 86.5 vs. 81.2%, Fig. 3) have stayed unchanged in spite of the increasing severity of disease of transplant recipients. This good result has been obtained thanks to optimized perioperative management with intensive collaboration of surgeons, hepatologists, anaesthesiologists and intensive care physicians of the transplant centre.

Fig.3: Liver transplantation USZ 2004- 09/2009

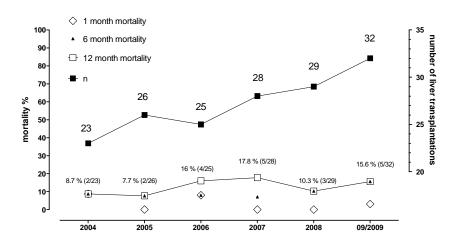


Fig. 4: MELD score at the time of liver transplantation prior and since amendment in July 2007

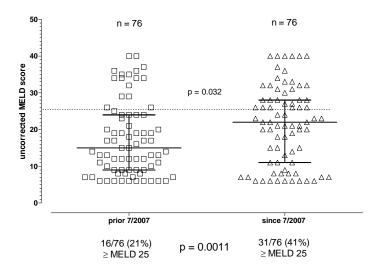
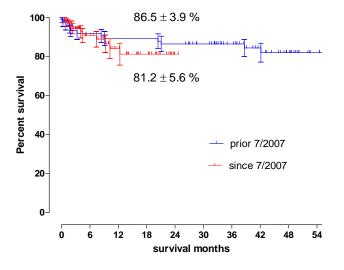


Fig. 5: Survival after liver transplantation prior and since amendment in July 2007



### 4.5. Kidney transplantation

Marc Schiesser

### **Clinical activities**

A total of 85 kidney transplantations have been performed in the year 2009. Of 85 transplantations 29 were living donor kidneys, and 5 transplantations were performed in children. Since the implementation of the new transplantation law in 2007 and the establishment of the method for the determination of HLA antibodies we have transplanted a growing number of high risk patients and patients with donorspecific antibodies. The immune suppression schemes have been adapted to that effect, and in spite of the increased risk we have obtained good results so far. For 2009 we would specifically like to mention the successful transplantation of a monozygotic twin couple without immune suppression as well as the transplantation of an organ with thin basement membrane disease. In addition we have an increasing number of patients on the waiting list with terminal renal insufficiency due to liver-, lung- or heart transplantation. The programme for ABO-incompatible kidney transplantation launched at the end of 2006 has been further developed and until now we have transplanted 15 patients with excellent patient and transplant survival. Furthermore a protocol for the desensibilization of patients with high risk antibodies has been established and approved by the ethics committee. The interdisciplinary monitoring of patients has been extended. The appointment of a clinical senior physician for the transplant centre has proved itself, and the attendance of the patients could be further optimized. The permanent availability of a clinical senior physician for the care, the patients and in his function as important link between the separate involved disciplines has turned out to be extremely helpful.

#### Research activities

A case series on steroid reduction in ABO-incompatible transplant patients has been published in collaboration with the University of Basle. In addition a murine kidney transplantation model has been established among others by the group of Prof. Fehr, by means of which the efficacy of new medicaments such as e.g. BCL 2 inhibitors can be tested by now. Moreover a 'mixed chimerism' model has been established, which allows the examination of allograft tolerance mechanisms. A retrospective analysis of the urologic complications and their management produced excellent results with regard to perioperative morbidity.

### 4.6. Pancreas transplantation

Markus K. Müller

Seven combined pancreas-kidney transplantations have been performed in 2009. This is a decrease compared to the previous year, which is primarily due to the lower number of appropriate donors. The interdisciplinary collaboration with colleagues from the nephrology and diabetology divisions is still excellent. The patients are jointly evaluated and determined preoperatively. Furthermore they profit from the specialized care of the transplant centre. In the course of the past year a proposal has been written in collaboration with Swisstransplant on behalf of the Federal Commission of Indemnification in order to secure a cost assurance for pancreas transplantation alone after preceding kidney transplantation (within the scope of living donor kidneys). The proposal has been submitted in the spring of this year.

## 4.7. Islet transplantation and diabetological care

Roger Lehmann

In 2009 five islet isolations have been performed all of which could be transplanted as islet after kidney transplantations. Since islet transplantation represents a minimally invasive intervention, patients are admitted in the emergency unit on ward E WEST and dismissed at any rate on the next day. Only combined transplantations are attended on the interdisciplinary ward.

During this year the trend toward marginal donor organs was even intensified, which in spite of optimized isolation technique and good enzymes resulted in a lower yield of high-quality islets, so that many offers had to be declined for medical reasons.

Research within the reporting period has been successful in several respects. The production of pseudo islets of a defined size by means of a technique pertaining to stem cell research (hanging drops) has led to promising results, which could be presented in several international meetings (ESOT Paris, IPITA Venice, FID Salzburg, Acrobat Workshop Dresden). In order to be able to produce a sufficient number of pseudo islets, a new disk has been developed and patented, which would allow treating complete islet isolations as pseudo islets. At present different disks and materials are being tested in order to obtain the best results. We have also started to test these islets in vivo. With this new technique we hope to help to significantly enhance the survival of islets in the liver and thus improve the results of islet transplantation. As already mentioned in the previous report, the diabetological attendance and organization of the interdisciplinary ward round of Visceral Surgery, Nephrology, Infectiology and Endocrinology/Diabetology on the new interdisciplinary ward have been significantly improved through the creation of the position of a clinical senior physician.

The interdisciplinary collaboration with regard to clinical kidney-pancreas transplantation has again been substantially improved in 2009. All patients scheduled for pancreas transplantation are summoned up by the Clinic of Endocrinology/Diabetology, where diabetes and metabolic regulation as well as consequential diabetic complications are evaluated and diabetes regulation is improved. In addition pros and cons of pancreas and islet transplantation are discussed with the patient and the respective procedure is thoroughly explained.

Planning is well advanced for the development of a new immune suppression protocol for combined islet-kidney and pancreas-kidney transplantation, which is supposed to eliminate steroids to a large extent, as well as to replace Rapamune in islet transplantation.

### 5. Attachments

## 5.1. Staff of the Transplant Centre

	Board	Curatorship
Management	Coordinator PD Dr. Markus Weber (till 02-28), Prof. Thomas Fehr (from 03-01)	Chairman Prof. Pierre-Alain Clavien
Heart	Prof. Georg Noll PD Dr. Markus Wilhelm	Prof. Thomas Lüscher Prof. Volkmar Falk
Lung	Dr Sarosh Irani (till 04-31), Prof. Annette Boehler (interim from 05-01) PD Dr. Sven Hillinger	Prof. Annette Boehler Prof. Walter Weder
Liver	PD Dr. Andreas Geier PD Dr. Philipp Dutkowski	PD Dr. Beat Müllhaupt Prof. Pierre-Alain Clavien
Kidney	Prof. Thomas Fehr Dr. Marc Schiesser	Prof. Rudolf Wüthrich Prof. Pierre-Alain Clavien
Pancreas and islet cells	Prof. Roger Lehmann PD Dr. Markus Müller	Prof. Giatgen Spinas Prof. Pierre-Alain Clavien
Stem cells	PD Dr. Urs Schanz	Prof. Christoph Renner (interim till 08- 31), Prof. Markus Manz (from 09-01)
Consultant services	PD Dr. Nicolas Müller, Infectiology PD Dr. Günther Hofbauer, Dermatology	Prof. Claus Buddeberg
Anaesthesiology	PD Dr. Marco Zalunardo	Prof. Donath Spahn
Care	Béatrice Biotti	Carmen Oggier
Transplant coordination	Werner Naumer	
Research	PD Dr. Rolf Graf	
Data manager	Uschi Schäfer	
Clinical manager	Andreas Käser	
Dean		Prof. Klaus Wilhelm Grätz

	International Advisory Board
Heart	Prof. Ernst Wolner, Vienna/Austria
Lung	Prof. Dirk van Raemdonck, Leuven/Belgium
Liver	Prof. Xavier Rogiers, Ghent/Belgium
Kidney	Prof. Ulrich Frei, Berlin/Germany
Pancreas and islet cells	Prof. Peter Friend, Oxford/Great Britain
Stem cells	Prof. Bob Lowenberg, Rotterdam/Niederlands
Anaesthesiology and intensive care	Prof. Christian Putensen, Bonn/Germany
medicine	

-		Regional Advisory Board
Bellinzona	Ospedale San Giovanni	Prof. Claudio Marone
Chur	Kantonsspital	Dr. Walter Brunner
Chur	Kantonsspital	PD Dr. Adrian Frutiger
Frauenfeld	Kantonsspital	Dr. Markus Hugentobler
Gais	Klinik Gais AG	Dr. Angelika Bernardo
Lachen	Spital	Dr. Andreas Hirlinger
Luzern	Kantonsspital	Dr. Claudia Hirschi
Münsterlingen	Kantonsspital	PD Dr. Thomas Neff
St. Gallen	Kantonsspital	PD Dr. Tim Gerlach
Winterthur	Kantonsspital	Dr. Thomas Kistler
Zollikerberg	Spital Zollikerberg	Dr. Jörg Bleisch
Zürich	Kinderspital	Prof. Oskar Bänziger
Zürich	Klinik Hirslanden	Dr. Marianne Stiner
Zürich	Stadtspital Waid	Prof. Patrice Ambühl

## 5.2. List of Network Hospitals

GZO Spital Wetzikon
Hirslanden Klinik Aarau
Kantonsspital Chur
Kantonsspital Frauenfeld
Kantonsspital Glarus
Kantonsspital Münsterlingen
Kantonsspital Schaffhausen
Kantonsspital Winterthur
Kantonsspital Zug
Kinderspital Zürich
Klinik Hirslanden Zürich
Klinik im Park
Kreisspital Männedorf
Spital Bülach
Spital Lachen
Spital Limmattal
Spital Luzern
Spital Schwyz
Spital Uster
Spital Zimmerberg
Spital Zollikerberg
Stadtspital Waid
Stadtspital Triemli

## 5.3. Transplantation activities 2008-2009

Transplantations performed

Organ	2008	2009
Heart total	9	9
- Heart and kidney	1	0
Lung total	25	26
Liver total	28	50
- NHBD single-liver	23	44
- Living donor liver	4	4
- Liver and kidney	1	2
Kidney total	83	85
- NHBD single-kidney	42	47
- Living donor kidney	29	29
- Kidney and pancreas	10	7
- Kidney and islet cells	0	0
- Kidney and heart	1	0
- Kidney and liver	1	2
Pancreas total	10	7
Islet cells total	7	5
Stem cells (allogeneic)	36	34

Multi-organ donations at the USZ

_Multi-organ donations at the USZ	2008	2009
Donors from USZ	8	1
Donors from network hospital	7	15

### 5.4. Publications

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### 5.5. Continuing education programme

### 5.5.1. Spring Symposium "Organspende" ("Organ Donation")

Frühjahres-Symposium-Programm 26.05.09

## 5.5.2. Autumn Symposium "Challenges in modern transplantation: elderly recipients and donors after cardiac death"

Herbst-Symposium-Programm 27.11.09

### 5.5.3. Monthly seminar "Hot topics in transplantation" (TNT)

TNT-Jahres-Programm 2009