Congrès conjoint francobritannique
de néphropédiatrie
1-3 Décembre 2016
Institut Imagine, Paris

Franco-British Paediatric Nephrology Meeting
1-3 December 2016
Institut Imagine, Paris

Hôpital Universitaire Necker-Enfants Malades
24, Bd du Montarnasse, 75015 Paris
This meeting has been kindly supported by educational grants from the following companies:

Ce congrès a reçu le soutien des compagnies suivantes:
DAY 1: Thursday 1st December 2016

Part 1: Introduction and transplantation

<table>
<thead>
<tr>
<th>Chairs</th>
<th>Christian Jacquelin (France); David Hughes (UK)</th>
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<tbody>
<tr>
<td>14h00-14h15</td>
<td>Welcome</td>
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<tr>
<td>14h15-14h30</td>
<td>Organisation of paediatric nephrology services in France</td>
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<tr>
<td>14h30-14h45</td>
<td>Organisation of paediatric nephrology services in UK</td>
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<tr>
<td>14h45-15h15</td>
<td>Paediatric transplant experience in France</td>
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<tr>
<td>15h15-15h45</td>
<td>Paediatric transplant experience in UK</td>
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15h45-16h15 oral communications:

Pre-emptive kidney transplantation is associated with improved graft survival in children: data from the French renal replacement therapy registry.

Mathilde Reydit, Bordeaux

Prophylaxie du cytomégalovirus après transplantation rénale chez l’enfant : vers un allongement de la durée de traitement? (Cytomegalovirus prophylaxis after kidney transplantation in children: longer is better.)

Alexis Rybak, Hôpital Robert Debré, Paris


Julien Hogan, Hôpital Robert Debré, Paris

Interest of epitope load for evaluating the HLA compatibility in pediatric renal transplantation.

Mélissa Ould Rabah, Hôpital Necker-Enfants Malades, Paris

16h15-16h45

Coffee break/posters/exhibitors
**Part 2: Steroid sensitive nephrotic syndrome**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker</th>
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<tbody>
<tr>
<td>16h45-17h00</td>
<td>Management of newly-presenting nephrotic syndrome in France</td>
<td>Claire Dossier</td>
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<tr>
<td>17h00-17h15</td>
<td>Management of newly-presenting nephrotic syndrome in UK</td>
<td>Nick Webb</td>
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<tr>
<td>17h15-17h30</td>
<td>Management of SDNS and Rituximab experience in UK</td>
<td>Rodney Gilbert</td>
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<tr>
<td>17h30-17h45</td>
<td>Management of SDNS and Rituximab experience in France</td>
<td>Vincent Guigonis</td>
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**17h45-18h15** oral communications:

- **Rituximab for frequently relapsing nephrotic syndrome or steroid dependent nephrotic syndrome: what is the lowest effective dose?**
  - Andrew Maxted, Nottingham

- **Effet secondaire du rituximab prescrit chez des enfants ayant un syndrome néphrotique. Etude rétrospective multicentrique.** [Adverse effects of rituximab used in children with idiopathic nephrotic syndrome. A multicentric retrospective study.]
  - Fanny Laliève, Limoges

- **Rituximab and intravenous immunoglobulin in the treatment of steroid-dependent nephrotic syndrome.**
  - Julien Hogan, Hôpital Robert Debré, Paris

- **Syndrome néphrotique congénital et infantile non-génétique : nouvelles approches diagnostiques et thérapeutiques.** (Non-genetic congenital and infantile nephrotic syndrome: new diagnostic and therapeutic management.)
  - Jean-Marie de Guillebon de Resnes, Robert Debré Hospital, Paris
### Part 3: Ethical issues in infancy

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
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<tbody>
<tr>
<td>09h00</td>
<td>Management of ESRD in infancy in UK</td>
<td>Heather Lambert</td>
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<tr>
<td>09h20</td>
<td>Management and ethical approaches in France</td>
<td>Rachel Vieux</td>
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<td>09h40</td>
<td>General discussion</td>
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<tr>
<td>10h00</td>
<td>oral communications:</td>
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<tr>
<td>10h00</td>
<td><strong>Cakutome</strong>, a high-throughput tool for molecular diagnosis and identification of novel causative genes for CAKUT patients</td>
<td>Laurence Heidet, Hôpital Necker-Enfants Malades, Paris</td>
</tr>
<tr>
<td>10h00</td>
<td><strong>French cohort of transient antenatal Bartter syndrome with MAGED2 mutations.</strong></td>
<td>Anne Legrand, Hôpital Européen Georges Pompidou, Paris</td>
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<tr>
<td>10h00</td>
<td><strong>A retrospective review of paediatric patients with Bartter and Gitelman syndrome.</strong></td>
<td>Patrick Walsh, Newcastle</td>
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<tr>
<td>10h00</td>
<td><strong>Fistule artério-veineuse par microchirurgie chez l’enfant de moins de 20 Kg : expérience monocentrique.</strong> [Autologous arteriovenous fistulae using microsurgery for hemodialysis in young children weighing 20 kg or less: single center experience.]. Vasiliki Karava, Hôpital Robert Debré, Paris</td>
<td>Vasiliki Karava, Hôpital Robert Debré, Paris</td>
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<tr>
<td>10h00</td>
<td><strong>A snapshot of acute kidney injury in tertiary paediatric centres in the United Kingdom.</strong></td>
<td>George Verghese, Liverpool</td>
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<td>10h00</td>
<td><strong>Time to STOP acute kidney injury.</strong></td>
<td>Amanda Newnham, Leeds</td>
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<tr>
<td>10h00</td>
<td><strong>Automated estimated GFR reporting in children using a height-independent formula.</strong></td>
<td>Andrew Lunn, Nottingham</td>
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<td>10h00</td>
<td><strong>Effect of nonsteroidal anti-inflammatory drugs in children with Bartter syndrome.</strong></td>
<td>Julien Hogan, Hôpital Robert Debré, Paris</td>
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**11h00-11h30**

Coffee break and poster session (tour)

### Part 4: Research and patient support

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<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker</th>
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<tbody>
<tr>
<td>11h30-11h45</td>
<td>Research themes in UK</td>
<td>Rachel Lennon</td>
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<tr>
<td>11h45-12h00</td>
<td>Research themes in France</td>
<td>Olivia Boyer</td>
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<tr>
<td>12h00-12h15</td>
<td>Patient support in France</td>
<td>Denis Morin</td>
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<tr>
<td>12h15-12h30</td>
<td>Patient support the UK</td>
<td>Michelle Rossiter</td>
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<tr>
<td>12h30-13h00</td>
<td><strong>Oral communications:</strong></td>
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<td></td>
<td><em>Inter-observer variability of the histological classification of lupus glomerulonephritis in children</em></td>
<td>Louise Oni, Liverpool</td>
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<td><em>Mycophenolic acid area under the curve is associated with therapeutic response in pediatric lupus nephritis.</em></td>
<td>Astrid Godron, Bordeaux</td>
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<td><em>Outcome following switch between brand name and generic tacrolimus in paediatric population.</em></td>
<td>Swetha Vijayan, Nottingham</td>
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<td><em>Evaluation des effets pharmacodynamiques d’une formulation innovante d’alcalinisants à libération prolongée sur les paramètres urinaires chez les sujets sains adultes. (Evaluation of the pharmacodynamics effects of an innovative prolonged release alkalinising formulation in the urine parameters in healthy adult subjects.)</em></td>
<td>Aurelia Bertholet-Thomas, Lyon (on behalf of Advicenne)</td>
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**13h00 - 14h30**

Lunch and poster session (tour)

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<tr>
<th>Time</th>
<th>Session</th>
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<tr>
<td>14h30-17h30</td>
<td>Small group meetings / free time</td>
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<tr>
<td>17h30-19h00</td>
<td>SNP general assembly</td>
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<td>BAPN business meeting</td>
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# Day 3: Saturday 3rd December 2016

### 08h00-08h45

Alexion breakfast symposium – see separate programme for details

### Part 5: CKD

<table>
<thead>
<tr>
<th>Chairs</th>
<th>Tim Ulinski (France) ; David Milford (UK)</th>
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<tbody>
<tr>
<td>09h00-09h30</td>
<td>Growth hormone use UK, France and Europe</td>
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<td>Jérôme Harambat</td>
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<td>09h30-10h00</td>
<td>Phosphate binders and calcium</td>
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<td>Lesley Rees</td>
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<tr>
<td>10h00-10h30</td>
<td>Bone disease</td>
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<td>Justine Bacchetta</td>
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### 10h30-11h00

Coffee break and poster session

### Part 6: What's new?

<table>
<thead>
<tr>
<th>Chairs</th>
<th>Mordi Muorah (UK), Rémi Salomon (France)</th>
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<tbody>
<tr>
<td>11h00-11h30</td>
<td>Genetics of glomerular disease</td>
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<td>Moin Saleem</td>
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<tr>
<td>11h30-12h00</td>
<td>Genetics of complement disorders</td>
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<td>Anne-Laure Sellier-Leclerc</td>
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<tr>
<td>12h00-12h30</td>
<td>Genetics of tubular disease</td>
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<td>Detlef Bockenhauer</td>
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<tr>
<td>12h30-13h00</td>
<td>Genetics of autosomal dominant tubulointerstitial disease</td>
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<td>Bertrand Knebelmann</td>
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<tr>
<td>13h00-13h15</td>
<td>Closing remarks</td>
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<td>Christine Pietrement</td>
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<td>David Hughes</td>
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## Speakers and Chairs

<table>
<thead>
<tr>
<th>Name</th>
<th>Position and Affiliation</th>
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<tbody>
<tr>
<td>Christine Pietrement</td>
<td>Professor of Paediatrics, Paediatric Nephrologist, CHU de Reims, SNP President</td>
</tr>
<tr>
<td>David Hughes</td>
<td>Consultant Paediatric Nephrologist, Glasgow and BAPN President</td>
</tr>
<tr>
<td>Rémi Salomon</td>
<td>Professor of Paediatrics, Paediatric Nephrologist, Hôpital Necker Enfants-Malades, Paris, SNP Vice-President</td>
</tr>
<tr>
<td>Christian Jacquelinet</td>
<td>Medical Director, Agence de la Biomédecine, Saint-Denis and Head of French ESRD REIN Registry</td>
</tr>
<tr>
<td>Martin Christian</td>
<td>Consultant Paediatric Nephrologist, Nottingham, BAPN Secretary</td>
</tr>
<tr>
<td>Marie-Alice Macher</td>
<td>Paediatric Nephrologist, Agence de la Biomédecine</td>
</tr>
<tr>
<td>Stephen Marks</td>
<td>Consultant Paediatric Nephrologist, Great Ormond Street London, Chair of Paediatric Sub-Group to UK Kidney Advisory Group</td>
</tr>
<tr>
<td>Claire Dossier</td>
<td>Paediatric Nephrologist, Hôpital Robert Debré, Paris</td>
</tr>
<tr>
<td>Nick Webb</td>
<td>Professor of Paediatric Nephrology, Manchester</td>
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<tr>
<td>Rodney Gilbert</td>
<td>Consultant Paediatric Nephrologist, Southampton</td>
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<tr>
<td>Vincent Guigonis</td>
<td>Professor of Paediatrics, Paediatric Nephrologist, CHU de Limoges, SNP Treasurer</td>
</tr>
<tr>
<td>Pierre Cochat</td>
<td>Professor of Paediatrics, Lyon and IPNA President</td>
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<tr>
<td>Jan Dudley</td>
<td>Consultant Paediatric Nephrologist, Bristol</td>
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<tr>
<td>Heather Lambert</td>
<td>Consultant Paediatric Nephrologist, Newcastle</td>
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<tr>
<td>Rachel Vieux</td>
<td>Professor of Paediatrics, Paediatric Nephrologist, CHU de Besançon</td>
</tr>
<tr>
<td>Rachel Lennon</td>
<td>Welcome Intermediate Fellow and Consultant Paediatric Nephrologist, Manchester, BAPN Research Secretary</td>
</tr>
<tr>
<td>Olivia Boyer</td>
<td>Associate Professor of Paediatrics, Paediatric Nephrologist, Hôpital Necker Enfants-Malades, Paris</td>
</tr>
<tr>
<td>Denis Morin</td>
<td>Professor of Paediatrics, Paediatric Nephrologist, CHU de Montpellier, ORKID President</td>
</tr>
<tr>
<td>Michelle Rossiter</td>
<td>Lay Representative to BAPN Executive Committee and Volunteer with British Kidney Patient Association</td>
</tr>
<tr>
<td>Jérôme Harambat</td>
<td>Professor of Paediatrics, Paediatric Nephrologist, CHU de Bordeaux</td>
</tr>
<tr>
<td>Name</td>
<td>Position and Institution</td>
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<tr>
<td>Lesley Rees</td>
<td>Professor of Paediatric Nephrology, Great Ormond Street Hospital, London</td>
</tr>
<tr>
<td>Justine Bacchetta</td>
<td>Associate Professor of Paediatrics, Paediatric Nephrologist, Hôpital Femme Mère Enfant, Hospices civils de Lyon, Bron</td>
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<tr>
<td>Tim Ulinski</td>
<td>Professor of Paediatrics, Hôpital d'Enfants Armand-Trousseau, Paris</td>
</tr>
<tr>
<td>David Milford</td>
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<td>Detlef Bockenhauer</td>
<td>Professor of Paediatric Nephrology, Institute of Child Health, London &amp; Consultant Paediatric Nephrologist, Great Ormond Street Hospital</td>
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<td>Bertrand Knebelmann</td>
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<tr>
<td>Mordi Muorah</td>
<td>Consultant Paediatric Nephrologist, Birmingham</td>
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14H30-14H45 : Etude sur le syndrome néphrotique RITUXIVIG, Julien Hogan
14H45-15H : Groupe de travail SNI, Vincent Guigonis
15H-15H10 : HNF1b et biocollection, Vincent Guigonis
15H10-15H20 : Néphropathie du purpura rhumatoïde, Christine Pietrement
15H20-15H25 : ECULISHU, Arnaud Garnier
15H25-15H30 : ZITHROSHU, Marc Fila
15H30-15H35 : PTLD post greffe, Marc Fila
15H35-1545 : Etudes à partir des registres REIN/Cristal, Jérome Harambat
15H45-15H50 : Rituximab post greffe, Gwenaelle Roussey
15H50-16H00 : Groupe de travail greffe rénale,
16H00-16H10 : Groupe de travail prénatal, Laurence Heidet
16H10-16H40 : Filière Orkid, Denis Morin
16h40-17H: Tests génétiques: indications, difficultés...., Rosa Vargas-Poussou
Social Events

**Thursday night 19h30-21h30: Welcome cocktail, on the roof of the Imagine Institut**

**Friday night: Dinner Cruise on the Seine, Port de la Bourdonnais,**

20h00 Boarding
21h00 Departure
23h30 Arrival

**To come from Imagine Institut:**

Bus 92 or 82 – Station Maine-Vaugirard. Direction Port de Champerret

Stop at station Bosquet-Rapp (8 strips, about environ 15 minutes)

Then walk during 5-8 minutes towards Eiffel Tower to the pontoon 4, port de la Bourdonnais
Programme social

Jeudi soir 19h30-21h30: Cocktail de bienvenue, sur le toit de l’Institut Imagine

Vendredi soir: Diner croisière sur la Seine, Port de la Bourdonnais,

20h00 Embarquement
21h00 Depart
23h30 Arrivée

Pour venir de l’Institut Imagine:

Bus 92 – Station Maine-Vaugirard / Direction Port de Champerret -> Descendre à Bosquet-Rapp (8 arrêts – environ 15 minutes).

Il faut ensuite suivre la Tour Eiffel – 5/8 minutes de marche jusqu’au ponton 4 du Port de la Bourdonnais.
Paediatric nephrology in France
Training in paediatric nephrology in France

Christine Pietrement, présidente de la Société de Néphrologie Pédiatrique, CHU de Reims, France

Things are changing, perhaps a reform will be held in 2017. I am going to explain the current system. After the Baccalaureat, our high school final exam, at 18 years old, students start medical studies. The first year is very competitive at university level. For example in my university in Reims there are 1400 students registered in the first year, but only 200 of them will accede to the 2nd year of medical studies. The first 3 years are mainly theoretical teaching, and the last three years are divided half with theory and the other half with hospital training. At the end of the sixth year, there is a new competition, at the national level. Depending of their ranking, students choose a medical speciality and the university where they will continue their formation for 4 to 5 years depending on the speciality. After their choice they become house doctors, work in hospital. They can prescribe medication under the responsibility of a doctor with a hospital appointment. They have a salary, and receive some theoretical formation. During their 4 years, they will have 8 different medical placements, some of them are mandatory to become a paediatrician such as paediatric emergency or neonatology. Most of the trainings are held in the chosen university hospital or in the small hospitals around. At the end of the 4 years, the house doctor has to defend a medical thesis to become a medical Doctor and a final report to get the speciality in paediatrics.

In France paediatric nephrology is not an officially recognised specialty, as for all the paediatric specialties except neonatology. Thus, for the administration, paediatric endocrinologists, paediatric neurologist and so on are all paediatricians. If a house doctor is interested in paediatric nephrology he usually chooses to spend one of his placements in another hospital where there is a large department of paediatric nephrology with dialysis and transplantation, for example in Paris, Lyon or Toulouse. He gets his theoretical formation with a specific diploma « Diplome d'université de néphrologie pédiatrique ». This diploma is organized at the national level, 124 hours total of theory. The students have to write a report and take a written exam to be admitted. Around 20 house doctors in paediatrics follow the course each year. When the future of the house doctor is to integrate a nephrology team with transplant or dialysis, the young doctor completes his formation with a two-year fellowship in a large department of paediatric nephrology.

Organisation of services in France

The French health care system is designed so that the healthcare is free for patients with chronic disease. The choice of the physician is free. You understand that paediatric nephrologist is not a certified job, thus one can be involved in paediatric nephrology at different levels from relapsing nephrotic syndrome to renal transplantation, in a small team among other paediatric specialties or for few hospitals in a specific paediatric nephrology department. The places where patient can have transplant, dialysis or kidney biopsy are all in university hospitals. Thus, there is at least a paediatric nephrologist in 28 different hospitals, 25 centres can treat patients with chronic peritoneal dialysis, 20 centres can perform chronic haemodialysis, and 16 can transplant.
The “Société de néphrologie pédiatrique”

The first unformal group of paediatric nephrologists was established in 1975 by Michel Broyer from Necker, the name of this group was “Le club de néphrologie pédiatrique”. In 1984 the group got an official association status, and in 2000 it has become the actual Société de néphrologie pédiatrique. Any paediatrician identifying himself as a paediatric nephrologist wants to be part of our society « La société de néphrologie pédiatrique ». The active board is made of a president, a vice-president, a treasurer, a secretary, a representant of the French speaking countries, elected for a three-year renewable mandate duration, and the president of the next year annual meeting. To become a member the candidate has to send a cover letter and a *curriculum vitae* to the president and has to be recommended by a paediatric nephrologist. The decision of admission is taken once a year during the general assembly, which is part of the annual congress of the society held usually at the end of the year. The members of the society meet also once a year in March for what we call « the paediatric nephrology seminar ». The Society is linked to the Société Française de Pédiatrie, the association of all the French paediatricians and to the adult nephrology association, the Société de néphrologie, dialyse et transplantation. Our society is divided in working groups: nephrotic syndrome, lupus, chronic kidney disease, HUS, their aim is to think about new research protocols, to write recommendations, among others. The society gets funds from the annual registration fees and from the industry at its annual congress. With this money the society encourages young physicians by sponsoring their participation to international congresses provided that they present an abstract of their work; indeed, the society encourages research through awards to the best abstracts at the annual congress. Besides, the society helps the working groups by reimbursing travel expenses. We are currently 75 members (contributions up-to-date). The society has a website. We communicate by email with a google group discussion list to exchange information or to take advice for difficult cases; there are about 150 registered persons in the list. Most of the centres also meet around once a month with their closest centres via video conferences.

**Resources:**

http://sfndt.org/sn/SNP/index.htm
Paediatric nephrology in the UK

Martin Christian, BAPN Honorary Secretary

Organisation of services in the UK
The national health service (NHS) is designed so that healthcare is free at the point of need. In the last decade health services for each of the four devolved nations (England, Scotland, Wales and Northern Ireland) have been commissioned separately. England accounts for the majority of the British population. Some highly specialised services are commissioned nationally but paediatric renal services are commissioned by region.

Paediatric nephrology in the UK began in Glasgow in 1950 with the first regional referral unit established by Gavin Arneill. The regional paediatric renal units in the UK have been established for at least 30 years. There are 13 units in total - one each in the devolved nations (Glasgow for Scotland, Cardiff for Wales and Belfast for Northern Ireland). London has two units (Great Ormond Street and Evelina – formerly Guy’s Hospital); elsewhere in England there are units in Southampton, Bristol, Birmingham, Nottingham, Leeds, Manchester, Liverpool and Newcastle. Ten of these units carry out transplantation, the remaining 3 partner with a neighbouring unit for the surgery but provide work-up and follow-up locally. There are 70 consultant paediatric nephrologists in the UK. Nowadays, all practice paediatric nephrology only but until 15-20 years ago, many still had a general paediatric commitment as well. Each centre has a multi-professional team with specialised nurses, dietitians and psychosocial team. In other hospitals, children with less complex kidney disease are cared for by general paediatricians with a nephrology interest in nephrology (“SPINs”). All units see some of their patients in local clinics, many of them in shared-care clinics with local SPINs. Network-delivered care is how the government would like to see specialised services provide quality care close to home.

Training in paediatric nephrology in the UK
After 5 years at medical school, newly qualified doctors must spend 2 years as foundation doctors to be fully registered with the General Medical Council (GMC). In their second foundation year, they can apply for specialty training. Paediatric training takes 8 years to complete. In year 5, some choose to apply for specialty training. This may mean moving to a new city. Those wanting to train in paediatric nephrology must spend at least 2 years in specialist training. Paediatric training is governed by the Royal College of Paediatrics and Child Health (RCPCH). At the end of successful training, they receive a Certificate of Completion of Training (CCT). From 6 months before their expected CCT date, trainees can begin applying for a consultant post.

The BAPN
The British Association for Paediatric Nephrology (BAPN) was established in the 1973 with 15 founding members. The only officer at that time was an honorary secretary. The BAPN was affiliated initially to the British Paediatric Association (which became the RCPCH in 1996). In 2010, members voted for it to become a division of the Renal Association. It now shares secretarial support with the RA and shares an annual academic meeting. The BAPN president is a trustee of the Renal Association. The current BAPN executive committee comprises a president, honorary secretary, treasurer, training advisory committee chair and officers for: research, registry and audit, clinical services, quality improvement & innovation. There is also an ordinary exec member (a new consultant), and representatives for trainees, SPIN consultants and
a lay member. These officers represent the different areas of work with which the BAPN is concerned.

**Resources**
BAPN website – [www.renal.org/bapn](http://www.renal.org/bapn)
RCPCH website – [www.rcpch.ac.uk](http://www.rcpch.ac.uk)
More on UK paediatric nephrology in IPNA Currents, May 2015 - [www.ipna-online.org/publications/ipna-currents/](http://www.ipna-online.org/publications/ipna-currents/)
Paediatric kidney transplantation. French experience.

MA Macher, Agence de la biomédecine, France

In France, a pioneer in the field, kidney transplantation (KTX) was developed from the early 60s. The first paediatric KTX occurred in 1969 in Hôpital des Enfants-Malades and this treatment became widespread in the 80s in parallel to technical progress of dialysis in this population. Currently, with a few rare exceptions, every child with end stage renal disease (ESRD) will be offered a KTX project.

Epidemiology of Paediatric ESRD patients: a small population with specificities

France has 64.7 million inhabitants among whom 15 million under age 18. The overall incidence of ESRD is 163 pmh with 10 799 new patients in 2014 including a growing population of patients over 45. The incidence of ESRD in the paediatric population, defined as children and adolescents less than 18 y, is stable over time, between 6 and 7 new patients per million age-related population (pmp) i.e. 88 in 2014. The distribution of the age groups is: 0 -4 years 20% 5-9 years 12%; 10-14 years, 26%; 15-17 years, 24%.

The main primary diseases are CAKUT (27%) and hereditary nephropathies (35%).

Over the last ten year, the overall KTX activity rate increased from 41.6 pmh to 52.4 pmh (2572 to 3486 +35%) with an increasing gap between the number of new patients registered and the number of KTX and a worsening shortage. Meanwhile, the paediatric KTX activity remained stable with a mean number of 100 paediatric KTX every year (89 to 120, 7, 8 pmp). Paediatric patients account for 3% of the new registered patients on waiting list (126/4735) and 3% of transplant patients 114/3486).

The global prevalence of ESRD in 2014 is 1194 pmh with 44% of transplant patients. The paediatric prevalence is 48 pmp (658 patients under 18) with 80% of transplant patients.

Donor types and allocation policy for paediatric recipients

Living donors KTX account for 10 to 30% of paediatric transplantations with an average of 20% in the last 5 years (20% in 2015). This proportion is low compared to that observed in other European countries as well as in Canada and in the USA. The majority of pediatric KTX are performed from deceased donors after brain death. Deceased donors after circulatory death are not currently harvested in paediatric patients neither allocated to paediatric recipients.

Since 1996, a high level of prioritization is given to paediatric recipients in the French organs allocation policies. Paediatric priority initially given to children and adolescents under 16 years was extended up to the age of 18 in 2008. Pediatric priority is prolonged after 18 years if RRT has started <18 years.

Paediatric recipients have a priority on the 2 kidney grafts from paediatric donors which cannot be allocated to an adult recipient unless there is no isogroupe or ABO compatible paediatric recipient. Both kidneys are allocated at national level. Recipients are ranked by a score taking into account matching HLA class I and class II, time on dialysis and on waitlist, FAG index (access facility to transplantation), distance between donor and recipient. FAG index is the number of paediatric potential donors over the last 5 years who had less than 3 HLA mismatches and no excluded antigen: the smaller the number of potential donors is the greater number of points to score.

Moreover, paediatric recipients have a limited priority on kidney grafts from donors aged 18 to 30 years. One of the kidneys is allocated to one recipient of the local team and
the second one is given to a paediatric recipient in the absence of priority recipient at local, regional or national level ("Super Ugence", full-immunized match, hypersensitized, multiple grafts or other regional priority).

**Access to renal transplantation for paediatric candidates.**
The probability of first wait-listing for paediatric patients starting renal replacement therapy between 2002 and 2014, was of 19% at the start of dialysis (pre-emptive registration), 73% at 12 months, 86% at 24 months and 94% at 60 months. The probability of KTX for paediatric patients registered between January 2010 and December 2015 was 55% at 12 months for all patients and 71% for patients on active list. Preemptive KTX were accounting for 16 to 29% of KTX in these last five years (26% for 2015). In other words, the median time on active waitlist before KTX was 6.3 months, though longer for groups B recipients (8.23 months) and for young children (0-2 years, 8.23 months 3-5 years, 7.21 months). The sensitized children, defined by having more than 85% incompatible donors rate among donors harvested in the last five years, have the most difficult access to KTX with a median waiting time of 32.3 months. There is an accumulation of these patients on the wait-list, accounting for 24% of the patients remaining on list at 1st January 2015. During the last 5 years, more than 80% of kidney grafts allocated to paediatric recipients came from pediatric donors, including 17% of donors less than 6 years.

**Survival rate after transplantation**
Graft survival after transplant grafts in paediatric recipients has improved over time. The graft survival rate was respectively at one and five year 82.5% and 67.3% for the 1985-1995 cohort, 93.1% and 67.8% for the 1996-2005 cohort and 93.9% and 85.6% for the 2006-2014 cohort. The long-term graft survival of living donor KTX is better: 73% versus 62% at 10 years for the 1985-2014 cohort. Early graft failure rate is higher for recipients and donors less than 2 years. Graft survival at 5 years and 10 years is also lower in recipients aged 18 and older highlighting the difficulties of the therapeutic compliance in adolescents and young adults and of the child-adult transition. For patients registered before the age of 18, the patient survival after KTX was 99% at 1 year, 97.1% at 5 years, 95.7% at 10 years and 94% at 15 years for the 1996-2006 cohort. KTX offers the best chance of survival. It increases the expected remaining lifetime by about 20 years depending on the considered age compared to a patient who would stay on dialysis throughout his life.

**Conclusion:**
With an average of 100 new candidates and 100 transplants per year, paediatric KTX is a small proportion of transplantation activity in France. Specificities of this population justify the care of children and adolescents by paediatric teams. Paediatric ESRD patients have a good access to the waiting list and to KTX. The priority given to children enables the allocation of optimal donors' grafts with a short median wait time. Nevertheless, several improvements are warranted:

- to increase the preemptive transplantations by an earlier registration on wait-list and by the development of living donor KTX
- To prevent sensitization, by better matching HLA class II of the first transplants. This goal is achieved in young adults thanks to a new attribution score. Nevertheless, the small size of the paediatric waiting list limits the possibilities of 0 mismatch Class II, and raises the question of a broader sharing of pediatric grafts, between the nearby countries.
La greffe rénale pédiatrique. Expérience française

MA Macher, Agence de la biomédecine

En France, pays pionnier en la matière, la transplantation rénale (TR) s’est développée à partir du début des années 60. La première TR pédiatrique a eu lieu à l’hôpital des Enfants-Malades en 1969 et ce traitement s’est généralisé dans les années 80 parallèlement aux progrès techniques de la dialyse. Actuellement, sauf exception, tout enfant ayant une insuffisance rénale chronique terminale (IRCT) va se voir proposer un projet de TR.

Epidémiologie de l’IRCT chez l’enfant : une petite population avec des spécificités

La France compte 64,7 millions d’habitants dont 15 millions âgés de moins de 18 ans. L’incidence globale de l’IRCT est de 163 pmh avec 10 799 nouveaux patients en 2014 dont une part croissance de patients de plus de 45 ans. L’incidence de l’IRCT dans la population pédiatrique, définie en France comme les enfants et adolescents âgés de moins de 18 ans, est stable au fil du temps entre 6 et 7 nouveaux patients par million de la population du même âge (pmp) soit 88 nouveaux patients en 2014. La répartition des classes d’âges est la suivante : 0-4 ans, 20% ; 5-9 ans, 12,13% ; 10-14 ans, 26,4% ; 15-17 ans, 24,5%. Les principales maladies rénales primitives sont les anomalies du développement des reins et des voies urinaires (27%) et les néphropathies héréditaires (35%).

Dans les 10 dernières années, l’activité globale de TR a augmenté passant de 41,6 à 52,4 pmh (2572 à 3486 greffes annuelles soit +35%) avec une augmentation du nombre de nouveaux inscrits plus rapide que celle du nombre de greffes et une pénurie croissante. Pendant la même période, l’activité de TR pédiatrique est restée stable avec une moyenne de 100 greffes/an (fluctuant entre 89 et 120;7,8 pmp). Les candidats pédiatrices représentent 3% des nouveaux inscrits sur la liste d’attente (126 sur 4735) et 3% des transplantés (114/3486).

La prévalence globale de l’IRCT est de 1194 pmh en 2014 dont 44% de patients transplantés. La prévalence pédiatrique est 48 pmp (658 patients de moins de 18 ans) dont 80% de transplantés.

Type de donneurs et règles d’attribution des greffons pour les receveurs pédiatriques.

La part des TR pédiatiques à partir de donneur vivant est en moyenne de 20% dans les 5 dernières années (20% en 2015). Cette proportion est faible par rapport à celle observée chez nos voisins européens ainsi qu’au Canada et aux USA. La majorité des greffes est réalisée à partir de donneurs décédés en mort encéphalique. Les donneurs décédés après arrêt circulatoire ne sont actuellement pas prélevés chez des donneurs pédiatiques ni attribués à des receveurs pédiatriques. Pour l’attribution des greffons rénaux de donneurs décédés, il existe depuis 1996 un niveau de priorité élevé pour les receveurs pédiatriques. La priorité pédiatrique, initialement accordée à des enfants et adolescents de moins de 16 ans, a été étendue aux moins de 18 ans en 2008. Pour les patients ayant débuté la dialyse avant l’âge de 18 ans, cette priorité est prolongée jusqu’à la greffe. Les receveurs pédiatiques bénéficient d’une priorité absolue sur les
greffons rénaux des donneurs pédiatriques qui ne peuvent être attribués à un receveur non pédiatrique qu’en l’absence de receveur isogroupe et de groupe compatible. Les deux reins sont attribués au niveau national avec un classement des receveurs par un score qui prend en compte le matching HLA classe I et classe II, la durée d’attente en dialyse, la durée d’attente sur la liste d’attente, l’indice de facilité d’accès à la greffe (FAG), la distance entre le prélèvement et la greffe. L’indice FAG correspond au nombre de donneurs potentiels pédiatriques dans les 5 dernières années ayant au moins 3 compatibilités et aucun antigène interdit pour le receveur. Moins ce nombre de donneurs potentiels est grand, plus le nombre de points au score est élevé. Il existe, par ailleurs, une priorité relative sur les donneurs âgés de 18 à 30 ans. Un des reins est attribuée à l’équipe locale de prélèvement, l’autre rein est attribué aux enfants en l’absence de receveur prioritaire au niveau local ou régional (super urgence, full-match immunisé, hyperimmunisé, greffes multiples, priorité régionale autre).

**Accès à la greffe des candidats pédiatriques.**

Avec ces règles d’attribution, La probabilité d’être inscrit sur la liste d’attente pour les patients pédiatriques débutant un traitement de suppléance entre 2002 et 2014 était de 19% au démarrage de la dialyse (inscriptions préemptives) puis respectivement 73%, 86%et 94% à 12 mois, 24 mois et 60 mois. La probabilité d’être greffé était de 71% à 12 mois pour les malades pédiatriques inscrits sur liste active (hors contre-indications temporaires) entre 2010 et 2015 et de 55% sur la liste active et inactive. Les TR préemptives représentaient 16 à 29 % des TR selon les années (26% en 2015). Autrement dit, la durée médiane d’attente sur liste active avant TR est de 6,3 mois. Elle est allongée pour les groupes B (8,23 mois) et pour les jeunes enfants (0-2 ans, 8,23 mois ; 3-5 ans, 7,21 mois). Le principal problème est celui des enfants hyperimmunisés, définis par un taux de greffons incompatibles supérieur à 85%, qui malgré la priorité dont ils bénéficient au niveau national sur les reins adultes et pédiatriques ont une médiane d’attente à 32,3 mois. Ces patients sont la seule catégorie de patients pédiatriques qui s’accumulent sur la liste représentant 24% des patients restants en liste au 1er janvier 2015.

Dans les 5 dernières années, plus de 80% des greffons attribués aux receveurs pédiatriques provenaient de donneurs pédiatriques dont 17 % étaient âgés de moins de 6 ans.

**Survie après greffe**

La survie des greffons aprèes greffe chez les receveurs pédiatriques s’est améliorée avec le temps avec une survie respectivement à 1 et 5 ans de à 82,5% et 67,3% pour la cohorte 1985-1995, 93,1% et 67,8% pour la cohorte 1996-2005 et de 93,9% et 85,6% pour la cohorte 2006-2014. La survie des greffons de donneur vivant est supérieure avec une survie à 10 ans de 73% versus 62% pour les donneurs décédés (cohorte 1985-2014). Le taux d’échec précoce est supérieur pour les receveurs de 0 à 2 ans et pour les donneurs de moins de 2 ans. La survie des greffons à 5 ans et 10 ans est diminuée chez les receveurs ayant 18 ans et plus au moment de la greffe, soulignant la difficulté de la compliance thérapeutique à cet âge et de la transition enfant-adulte. Pour les patients inscrits sur liste avant l’âge de 18 ans, la survie après greffe est de 99% à 1 an, 97,1% à 5 ans, 95,7% à 10 ans et 94% à 15 ans pour la cohorte 1996-2005. La TR est la modalité de traitement de choix car elle augmente l’espérance de vie d’environ 20 années en fonction de l’âge considéré par rapport à un patient qui resterait toute sa vie en dialyse.
Conclusion.
Avec une moyenne de 100 nouveaux candidats et 100 greffes par an, la transplantation rénale pédiatrique représente une faible part de l’activité de greffe en France avec des spécificités qui justifient la prise en charge des enfants et adolescents par des équipes pédiatriques. La priorité accordée aux enfants permet l’attribution de greffons optimaux avec des moyennes d’attente faibles.

Les objectifs d’amélioration sont
- L’augmentation des greffes préemptives grâce à une inscription sur liste plus précoce et au développement des greffes à partir de DV
- La prévention de l’immunisation par l’amélioration du matching HLA classe 2 des premières transplantations. C’est l’objectif des modifications récentes du score d’attribution adulte. La petite taille de la liste d’attente pédiatrique limite les possibilités 0 mismatch classe 2 et ouvre la question sur une mutualisation plus large des greffons pédiatriques entre les pays proches.
- La création de filières plus structurées pour la transition vers les équipes d’adultes afin de combattre les échecs tardifs associés à cette période.

Références
Paediatric transplant experience in UK

Dr Stephen Marks, Consultant Paediatric Nephrologist

Clinical outcomes and research output from both living donors and deceased donors (donation after brain death and donation after cardiac death [DCD]) for paediatric renal transplant recipients (pRTR) in the United Kingdom are monitored with data provided from the National Health Service Blood and Transplant (NHSBT) and benchmarked against international centres of excellence. The kidney allocation scheme for deceased donors is currently being revised with points scoring scheme for both kidneys introduced in 2006 and the local and regional DCD scheme commenced in 2014. Ten of thirteen paediatric nephrology centres in the United Kingdom provide renal transplantation services (with the remaining three centres providing follow-up after renal transplantation). Latest data show 60% of pRTR are male with median age of 10 years and from 1991 to 2016 there has been an increase in ethnic minority recipients (from 15% to 33%) and sensitised patients (from 2% to 7%). The increase in living donation has seen a decrease in the paediatric kidney waiting list from 85 to 69 patients from 2000 to 2016. There has been recent research publishing the UK National Registry Study of kidney donation after circulatory death for paediatric recipients as well as the influence of living donation and HLA matching on long term renal allograft outcomes. Further research is ongoing in understanding outcomes of declined deceased donor offers with plan for a prospective study looking at the Access to Transplantation and Transplant Outcome Measures in Children (ATTOMic) study.
Management of newly-presenting nephrotic syndrome in France


Incidence of Idiopathic Nephrotic Syndrome in France remains stable over years. Regional studies have shown an annual incidence ranging from 1.7 and 3.4 new cases/100 000 children under 16 years old.

**French protocol** At initial presentation, patients are usually hospitalized in a general pediatric department or a pediatric nephrology department. Initial management consists in excluding differential diagnosis, starting symptomatic and specific treatment and providing treatment education to child and parents. Patients are usually discharged when urinary dipstick turns negative or when educational program is completed.

Since the 70es, the French “Société de Néphrologie Pédiatrique” has proposed a common protocol which is extensively applied in France. At first presentation, patients receive an 18-weeks course of oral prednisone according to the following schedule: 60mg/m²/day (maximum 60mg) divided in 2 doses for 4 weeks, followed by 60mg/m² on alternate days for 8 weeks, 45mg/m² on alternate days for 2 weeks, 30mg/m² on alternate days for 2 weeks and 15mg/m² on alternate days for 2 weeks, resulting in a cumulative steroid dose of 3990mg/m². Younger patients may receive oral prednisolone to facilitate oral intake.

Children exhibiting persistent proteinuria after 4 weeks of oral prednisone receive 3 IV pulses of methylprednisolone 1g/1.73m², with a success rate of 45% (NEPHROVIR cohort).

Indications for performing renal biopsy at diagnosis are age <1 or >12 years old, or atypical clinical or biological features, otherwise renal biopsy is only performed later in case of steroid resistance.

**Definitions** Nephrotic syndrome is defined by proteinuria > 0.20 g/mmol of creatininuría (or >2g/g) or > 50mg/kg/day and albuminemia <30g/l. Remission is defined by proteinuria < 0.02g/mmol of creatininuría (or <0.02g/g) or <5mg/kg/day. Steroid resistance is defined by the persistence of nephrotic proteinuria 8 days after the 3 MP pulses. In case of partial remission with proteinuria ranging from 0.10 to 0.20g/mmol, renal biopsy should also be discussed.

**Results** A region-wide prospective and population-based study conducted in the Paris Area provides recent results from the French protocol (NEPHROVIR cohort, N=188). 93% of patients are steroid sensitive, and 7% steroid resistant. Among steroid sensitive patients, 6% required intraveinous steroid pulse to obtain remission. Relapse-free rate for steroid sensitive patients are 40% at 12 months, 30% at 24 months and 20% at last follow-up. Steroid dependency occurs in more than 50% of steroid sensitive patients and at 5-years more than 50% of steroid sensitive and more than 2/3 of steroid dependant patients are still receiving one or more immunosuppressive drugs. In this French population, delay to first remission is not predictive of further relapse. Conversely, age at onset < 4 years is associated with a higher frequency of relapse, steroid dependency and long lasting therapies.
Discussion The challenge of treating newly presenting nephrotic syndromes is not only to obtain remission, but also to prevent further relapses and steroid dependency, which comes along with a long lasting disease course and morbidity. A study protocol with 6 months of levamisole in association to the steroid course should begin in the Paris Area in early 2017 (NEPHROVIR-3). Factors associated to a worse outcome should also probably be taken into account in future steroid protocols.


Management of steroid dependant nephrotic syndrome and rituximab experience in the SNP network

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While the management of a first flare of idiopathic nephrotic syndrome (INS) is identical in all pediatric centres in France, there is no single therapeutic strategy across the Société de Néphrologie Pédiatrique (SNP) network for steroid dependent nephrotic syndrome. An official guideline (“National Protocol of Care”) has been edited by the SNP for the treatment of idiopathic nephrotic syndrome, based on the current literature data. However, while these guidelines precisely explain the treatment of the first flare, they only mention and explain treatments that can be used when dealing with a SDNS, leaving the decision to pediatric nephrologists for the best therapeutic sequence to choose in each cases. As expected, levamisole, mycophenolate, calcineurin inhibitors, cyclophosphamide and rituximab (RTX) are treatments cited by these guidelines, but no specific ranking is proposed for these therapies.

In order to give an actual picture of the current therapeutic strategies used across the SNP network for patients presenting with steroid dependent nephrotic syndrome (SDNS), a survey was sent to SNP members through a mailing list. All members of the SNP network were invited to answer and, therefore, several answers could be posted from the same centre. Results of this survey are presented below.

61 answers of senior physicians were collected from 32 different centres (France, Switzerland, Saudi Arabia). 85% of the responders had more than 5 years of experience in the field of pediatric nephrology and 74% worked in a unit with kidney graft activity.

It was asked to rank the order of use of the usual steroid sparing agents for two different cases: a four years or 14 years old patient presenting with SDNS. Based on the answers received, the mean position of each treatment was as follows. For the 4 years old patient: Steroids > Mycophenolate > Levamisole > Cyclosporine > Tacrolimus > Rituximab > Cyclophosphamide. For the 14 years old patient: Mycophenolate > Steroids > Tacrolimus > Cyclosporine > Levamisole > Rituximab > Cyclophosphamide.

Three percent of responding physicians (n=2) had never used RTX for INS. Date of first use of RTX for the remaining physicians ranged from 2005 to 2015. Fifty nine percent and 26% of responders to the survey had treated less than 10 and between 10 and 20 cases each, respectively. In 87% of cases, indications of RTX were validated in a collegial manner. Based on an ongoing retrospective study, it is has been extrapolated that between 450 and 500 children have been treated with RTX for INS in France since 2005 (recurrence on kidney grafts excluded).

On a 4 levels scale, RTX was considered as effective (level 3/4) or very effective (level 4/4) for 28 and 72% of responders respectively. Opinions differ more widely as regards the safety of RTX: 55% answered to this question with the two lower marks (1/4 or 2/4) on a similar 4 levels scale.

The main indication for RTX was SDNS (93%), followed by steroid resistant nephrotic syndrome (SRNS) responsive to calcineurin inhibitors (57%), post graft recurrence (52%), SRNS irresponsive to calcineurin inhibitors and prevention of post graft recurrence (38% each). Only 6 participants (10%) had already use RTX for the
treatment of a first flare of INS. For SDNS, main indications were based on adverse effects or lack of efficacy of steroid sparing agents (96%) and poor adherence to oral treatment (74%). The first course of RTX was composed by two 375 mg/m² infusions in 52% of cases and one single infusion in 23% of cases. In the remaining cases, the number of infusion was linked to the date of B cell depletion occurrence.

Considering the therapeutic strategy after a first course of RTX in a 5 years old patient with SDNS, 61% repeatedly infused RTX for 12 to 24 months (most of the time accordingly to CD19 cells levels), 35% switched back to MMF therapy and 3% administered therapeutic doses of IVIg to RTX. When the same question was asked for a 15 years old patient answers were 78%, 19% and 3%, respectively.

Prophylactic antibiotic treatment (Sulfamethoxazole + Trimethoprim) was systematically prescribed in 61% of cases, and in 25% of cases only if other immunosuppressive treatments were associated to RTX. Substitutive infusions of IVIg were administered accordingly to plasma IgG levels in 70% of cases, never in 13%.

Finally, risks of infection, infusion related adverse effects, and – to a lesser extent – risk of neutropenia were the more frequent adverse effects discussed with patients and family. In the other hand, JC virus infection, risk of VHB reactivation and risk of Stevens Johnson syndrome were the less frequently discussed.

Beyond providing a snapshot of current use of RTX within the SNP network, these data also highlight potential clinical research questions that could be addressed in the future.

Acknowledgments to: the members of the SNIF and SORARE groups that helped to design and validated the survey and to all members of the SNP network who answered to this survey.

Conflict of interest. V Guigonis is principal investigator of a prospective trial evaluating the efficacy of RTX on INS, partly funded by Roche Laboratories.
Neonatal renal replacement therapy: more than a technical challenge, a multidisciplinary and ethical reflection for a crucial decision
Erika LINDER, MD, Antoine BURGUET, MD PhD, François NOBILI, MD, Rachel VIEUX, MD PhD

Background. Technological advances in foetal and neonatal medicine, recent changes in French legal framework, and the encouraging results of the long-term outcomes in children with neonatal renal failure provide elements to an ethical reflection.

Subjects and methods. We led a nationwide enquiry amongst French paediatric nephrologists, intensivists and neonatologists, exploring decision making process to start renal replacement therapy (RRT) or to deliver palliative care to neonates or infants with pre- or end-stage renal disease; and ethical quandaries at hand in such scenarii.

Results. 134 answers with a complete national coverage were obtained. Care to be delivered to an infant in pre- or end-stage renal disease was not consensual. Paediatric nephrologists were more prone to initiate a dialysis/graft program than paediatric intensivists. When chronic kidney disease was associated with comorbidities, especially neurological impairment, physicians regardless of their subspecialty were more reluctant to conservative treatment. Many surveyed doctors did not give their opinion in these antenatal and/or postnatal situations, considered as unique and justifying a multidisciplinary reflection.

Conclusion. Such ethical dilemmas are sore for parents and physicians. They can only be overcome by the requirement to take into account, both concrete on-the-ground realities and general principles and values acknowledged to be a basis for the respect of the person. In this way, it ensures the humanity and the humanisation of a practise that needs to confront items of different nature, which cannot be amalgamated. The answer is not simple; it is always unique and can only be approached by a multidisciplinary, time-consuming, open discussion which will never erase uncertainty.
Epuration extra-rénale néonatale :
plus qu'un défi technique, une réflexion multidisciplinaire pour une décision cruciale

Erika LINDER, MD, Antoine BURGUET, MD PhD, François NOBILI, MD, Rachel VIEUX, MD PhD

Contexte. Les progrès techniques de la médecine fœtale et néonatale, l'évolution récente du cadre juridique, ainsi que les résultats encourageant du suivi à long terme des enfants en insuffisance rénale néonatale nourrissent les réflexions éthiques.

Objectif. Décrire, par l'intermédiaire d'un questionnaire informatique adressé aux néphropédiatres, réanimateurs néonatologues et pédiatres français, l'évolution des points de vue et des pratiques médicales sur la dernière décennie dans le cadre de l'épuration extra-rénale en période néonatale.

Résultats. 134 réponses couvrant l'ensemble du territoire français ont été obtenues. Les soins à délivrer à un nourrisson en insuffisance rénale préterminale ou terminale n'étaient pas consensuels. Les néphropédiatres étaient plus favorables à initier un programme de dialyse/transplantation que les réanimateurs pédiatres. Lorsque des comorbidités, notamment neurologiques, se surajoutaient à la maladie rénale chronique, les médecins quelle que soit leur surspécialité, étaient plus réticents à un traitement conservateur. Plusieurs médecins ne se prononçaient pas dans certaines situations pré- ou post-natales, jugées comme uniques et relevant d'une réflexion multidisciplinaire.

Conclusion. La prise en charge curative ou palliative de ces nouveau-nés, lourde et coûteuse, est un dilemme éthique dépendant de données médicales mais également familiales, économiques, sociétales et liées au médecin lui-même. La prédiction d'un pronostic, intrinsèquement incertaine, doit être prise en considération lors des discussions avec les parents. Les possibilités techniques actuelles ne devraient pas occulter l'importance de la réflexion éthique. Chaque situation est unique. Ces décisions, cruciales, nécessairement collégiales et prenant pleinement en considération le projet parental, devraient être prises dans l'intérêt supérieur de l'enfant.
Patient support in France

Denis Morin, CHU Montpellier, Filière ORKiD

The aids provided in France for children with chronic kidney diseases aim to allow an easy access for care and diagnosis, a 100% financial support for hospital care (and homecare if necessary), a financial assistance for children having a significant degree of disability, an easy schooling for patients whatever their age and whatever their pathology, a psychological support, the provision of informations easy to understand, the contact with other patients having the same disease within patient's associations... All of this to allow a good quality of life despite health conditions that would justify a medical support "for life".

Different public agencies, medical units and patients associations are involved in this field:

1 – The Social Security service: the care of these children regarding their pathology are financially supported 100% with the ALD 30 program (ALD: long-term pathology), for hospital care and for homecare, whatever their treatments.

2 - The MDPH (Maison Départementale du Handicap) which provides financial aids for parents (parental presence allowance, allowance for handicapped child...)

3 - The "Education Nationale" in conjunction with the school's services at hospital that aims to facilitate the education of children while pursuing quality treatments. If necessary by implementation of PAI (welcome individual project in school) or with an assistance (eg AVS: helper for school life)

4 – Centers for diagnosis and treatments: there are pediatric nephrology units in each university hospital, with pediatric dialysis units and transplant centers for children in most of them. They are organized into centers of reference and competence and they work in regional and national networks to optimize the diagnosis and care of patients. In theses centers, multidisciplinary educational programs are organized as well as the transition toward adult's units.

5 - Patient associations: they have an important role in the transmission of information to patients and familie's in the fields of care, research as well as in the social aspects. Information meetings on different themes are regularly organized at the local, regional or national levels. Others information media exist such as website, booklet, newsletters, ...

So there are multiple opportunities for aid that, however, need to be coordinated and well used for each children, that is not often so simple... Above all, the social services and the medical team have to ensure the proper use of aid and the good coordination between the various agencies and services.

At a national level, the ORKiD (Orphan kidney disease) network for renal rare diseases, working closely with patient associations and all the pediatric nephrology units, has a role of coordination and stimulation of the different national agencies to best meet the daily needs of children and their families.
Aides aux patients en France

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Les aides prévues en France pour les enfants porteurs de pathologies rénales chroniques visent à permettre un accès au soin et au diagnostic faciles, la prise en charge financière des soins à l'hôpital (comme à domicile si cela est nécessaire), l'obtention d'aides financières pour les parents d'enfants porteurs d'un degré de handicap significatif, la scolarisation des enfants quel que soit leur âge, un soutien psychologique, la mise à disposition de supports d'informations, la mise contact avec d'autres patients porteurs de la même pathologie,...Il s'agit de leur permettre une vie aussi facile et remplie que possible malgré l'existence d'une pathologie pouvant justifier une prise en charge "à vie".

Différents organismes, hôpitaux et associations interviennent pour mettre en place ces aides :

1 – La Sécurité sociale : les soins de ces enfants relatifs à leur pathologie sont pris en charge à 100% dans le cadre du programme ALD 30, que ce soit pour les soins hospitaliers comme pour les traitements à prendre à domicile, quels que soient ces traitements.

2 – La MDPH qui permet d'obtenir des aides financières pour les parents (allocations de présence parentale, allocation enfant handicapé,...)

3 – L'Education Nationale en lien avec les services de l'école à l'hôpital avec pour objectif de faciliter la scolarisation des enfants tout en poursuivant des traitements adaptés avec si nécessaire mise en place de PAI et obtention d'une aide à la scolarisation (AVS par exemple)

4 - Centres de soins et de diagnostics : il existe dans chaque CHU des services de néphrologie pédiatriques. Ils sont organisés en Centres de références et de compétences et ont l'habitude de travailler en réseaux régionaux et nationaux, permettant d'optimiser le diagnostic, les soins aux patients et la recherche. Il y a en particulier des centres de dialyse et de transplantation pédiatriques. Dans ces centres, sont organisées des actions d'éducations thérapeutiques et la transition vers les centres de néphrologie pour adultes y est organisée

5 – Les Associations de patients : elles ont un rôle important dans la transmission de l'information aux patients et à leurs familles dans les domaines du soin, de la recherche comme dans les aspects médico-sociaux. Des réunions d'informations sur différents thèmes et à visée locale, régionale ou nationale sont régulièrement organisées. D'autres supports d’information existent : site internet, livret, journal,...

Il existe donc différentes possibilités d'aides qui doivent cependant être coordonnées et bien utilisées. C’est avant tout le rôle de l’équipe médicale et des services sociaux que de s'assurer de la bonne sollicitation des aides et de la coordination entre les différents intervenants.
A un niveau plus global, la filière des maladies rénales rares ORKiD (Orphan kidney disease), en lien étroit avec les associations de patients et les unités de néphrologie pédiatrique, a un rôle de coordination et de stimulation des différents organismes nationaux afin de répondre au mieux aux besoins quotidiens des enfants et de leurs familles.
The demise of calcium based phosphate binders – Is this appropriate for children?

Professor Lesley Rees, Great Ormond Street Hospital, London

Phosphate has probably the best described spectrum of toxicity of all molecules that circulate in excess in CKD. Decreased renal phosphate excretion plays a major role in the onset of hyperparathyroidism. Exposure of VSMCs to media containing elevated levels of phosphate induces a change to an osteoblastic phenotype and calcification occurs. Most importantly, plasma phosphate levels are positively and independently correlated with an increasing risk of death from cardiovascular disease. However, despite these clear associations, control of our patients’ plasma phosphate is one of our most challenging management issues, and indeed some physicians believe that a high plasma phosphate is an inevitable consequence of CKD, accepting that good phosphate control is an impossible task.

Hyperphosphataemia is very common in CKD, and particularly so in patients on dialysis. Phosphate control begins with dietary restriction, but as CKD becomes more severe this is rarely adequate and phosphate binders become necessary. Unfortunately, compliance with phosphate binders is poor, due to their side effects and to the repetitive monotony of the need for their ingestion with every meal and snack.

Phosphate binders are divided according to whether they are calcium based or calcium-free. There is an ongoing market for non-calcium containing binders, with new ones currently on trial. This is because of the recognition that phosphate control is difficult and remains poor, and the relationship that has been demonstrated in adults between gastrointestinal absorption and retention of calcium excess, and vascular calcification. However, only calcium carbonate and acetate are licensed in children, along with sevelamer hydrochloride for those over 12 years of age.

The growing skeleton is particularly vulnerable to the effects of CKD-MBD as calcium accrual in the skeleton continues from birth until peak bone mass is reached at approximately ~30 years of age. Calcium deficiency can occur as calcium intake and absorption and vitamin D levels may be low. On the other hand, high calcium levels, particularly in association with a high phosphate, can lead to arterial calcification, even in children. However, not all hypercalcaemia is due to excessive calcium intake.

In adults receiving dialysis, randomized trials have shown that the progression of calcification is greater with calcium acetate compared to a calcium-free binder sevelamer. These studies have led to recommendations to restrict the use of calcium-based phosphate binders. Importantly, the average age of patients in these studies was 65 years, with many being post-menopausal. Data from adult CKD-MBD studies should not be extrapolated to paediatric practice, but many paediatricians increasingly use calcium-free phosphate binders in children.

In this talk I will discuss the role of calcium in CKD-MBD, and the relative merits of calcium based and non-calcium containing phosphate binders in children.
Bone disease in children with chronic kidney disease

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Growth retardation, decreased final height and renal osteodystrophy (ROD) are common complications of childhood chronic kidney disease (CKD), resulting from a combination of abnormalities in the growth hormone (GH) axis, vitamin D deficiency, hyperparathyroidism, hypogonadism, inadequate nutrition, cachexia and drug toxicity.

The impact of CKD-associated bone and mineral disorders (CKD-MBD) may be immediate (serum phosphate/calcium disequilibrium) or delayed (poor growth, ROD, fractures, vascular calcifications, increased morbidity and mortality). Not only do these complications impact overall quality of life through their effects on both physical and mental well-being in children with CKD, but alterations in mineral metabolism and bone disease are linked to cardiovascular disease, the leading cause of death in children with CKD.

The bone and growth consequences of CKD have been highlighted in a cohort of 249 young Dutch adults with onset of end-stage renal failure before the age of 14 years: in this cohort, 61% of patients had severe growth retardation, 37% severe bone disease (as defined by at least one of the following conditions: deforming bone abnormalities, chronic pain related to the skeletal system, disabling bone abnormalities, aseptic bone necrosis and low-traumatic fractures) and 18% disabilities resulting from bone impairment.

More recently, fracture histories were obtained at baseline as well as at years 1, 3, and 5 in the prospective CKID cohort including 537 children with CKD. At enrollment, median age was 11 years, and 16% of patients reported a past of fracture. Over a median of 3.9 years, 43 boys and 24 girls presented with incident fractures, corresponding to 395 (95% confidence interval [95% CI], 293-533) and 323 (95% CI, 216-481) fractures per 10,000 person-years, respectively. These rates were 2- to 3-fold higher than published general pediatric rates. By multivariable analysis, advanced pubertal stage, greater height Z-score, walking difficulties, and higher PTH levels were independently associated with greater fracture risk; interestingly 25-D levels did not correlate with fracture risk. Phosphate binder treatment (predominantly calcium-based) was associated with lower fracture risk (hazard ratio, 0.37; 95% CI, 0.15-0.91; P=0.03). Participation in more than one team sport was associated with a higher risk of fracture.

Bone biopsy from the anterior iliac crest (after double tetracycline labeling) remains the reference standard to evaluate bone status in CKD patients. Even though it is rarely performed in clinical practice, bone biopsy followed by histomorphometry analysis are the only available techniques leading to an accurate evaluation of ROD. ROD is characterized by alterations in bone turnover, mineralization and volume; these three components should be evaluated independently to characterize the different subtypes of ROD, as defined by the K-DIGO in 2006. High bone turnover (secondary hyperparathyroidism, osteitis fibrosa cystica) is the primary skeletal lesion of pediatric ROD, and is present in virtually all untreated incident pediatric dialysis patients. This
lesion is caused by a long-term exposure to high serum PTH levels and 1,25(OH)2vitamin D deficiency. By contrast, low turnover lesions (i.e., adynamic bone disease) may occur as a result of excess treatment with vitamin D analogs and calcium salts and are characterized by relative low PTH and alkaline phosphatase levels as well as high serum calcium levels. Low bone turnover has been associated with an increased risk of vascular calcifications, fractures and more severe growth retardation. Defects in skeletal mineralization are also prevalent in pediatric patients with CKD—occurring in 30% in stage 2 CKD and increasing in prevalence as CKD progresses, even though bone turnover remains normal in the earliest CKD stages and becomes apparent while GFR decreases. In contrast to adult patients, nearly 80% of pediatric dialysis patients display some defect in skeletal mineralization, a problem that is not corrected by traditional therapy with vitamin D sterols and phosphate binders. Although alterations in skeletal mineralization (i.e. rickets) contribute to increased fracture rates, bone deformities, and growth retardation in children with normal renal function, their exact role in these clinical symptoms in children with CKD, remains to be elucidated.

Other diagnosis tools for pediatric ROD have been developed: if Dual X-ray Absorptiometry (DXA) is no longer recommended for the follow-up of pediatric CKD, innovative bone imaging techniques help physicians to better understand ROD, for example High Resolution peripheral Quantitative Tomography (HR-pQCT) or MRI. We recently performed HR-pQCT in a single-centre study of 32 teenagers with CKD, at the ultradistal tibia; as such, we assessed volumetric bone density (vBMD), microarchitecture, but also cortical porosity Ct.Po and mechanical properties with finite element analysis techniques (FEA). 32 CKD teenagers were compared to healthy peers, after matching on age, gender and pubertal stage on a 1/1 basis. CKD patients displayed significantly greater corrected calcium, PTH and 25-D levels than controls: 2.45 (2.28-2.68) vs 2.27 (2.14-2.42) mmol/L, 81 (9-359) vs 18 (9-34) pg/mL, and 70 (32-116) vs 60 (31-123) nmol/L, respectively (all p<0.05). Total and cortical bone areas were significantly lower in CKD patients: 585 (337-968) vs 626 (442-956) mm², and 66 (35-121) vs 82 (26-170) mm², respectively (both p<0.05). Conversely, Ct.Po, volumetric vBMD (total, trabecular and cortical), FEA-derived stiffness and failure load were not different between patients and controls. Thus, our results seemed quite reassuring in terms of bone status in CKD teenager, whereas others have described impaired cortical porosity in CKD. These discrepancies could be explained, at least partly, by the satisfying PTH control observed in this cohort.

The clinical management of CKD-MBD in children is currently focused on three main objectives: 1/ to provide an optimal growth in order to maximize the final height with an early management with recombinant GH therapy when required, 2/ to equilibrate calcium/phosphate metabolism so as to obtain acceptable bone quality and cardiovascular status, and 3/ to correct all metabolic and clinical abnormalities that can worsen bone disease, growth and cardiovascular disease, i.e., metabolic acidosis, anemia, malnutrition, and 25-D deficiency. All the following measures are used by pediatric nephrologists to optimize the CKD-MBD management: correction of hyperphosphatemia (dietary restriction of phosphorus, calcium-based phosphate binders, non-calcium based phosphate binders, notably sevelamer but also maybe in a next future iron-based phosphate binders), correction of 25-D deficiency, correction of hypocalcemia, and correction of hyperparathyroidism (vitamin D analog, calcimimetics, and exceptionally in 2016 parathyroidectomy). Native vitamin supplementation and
active vitamin D analogs are currently the mainstay of therapy for ROD in CKD children, decreasing PTH levels whilst increasing FGF23 levels. However, over-suppression of PTH levels in dialyzed children using vitamin D analogs may lead to adynamic bone disease, growth failure, cardiovascular calcifications, and growth plate inhibition.

Last, some orphan renal diseases, for example primary hyperoxaluria or nephropathic cystinosis, may also induce bone complications per se, therefore complicating the clinical picture and the clinical management of such patients.

The aim of the talk is to provide an overview of bone disease in pediatric CKD, from diagnosis to global management.

References


Genetics of tubular disease

Detlef Bockenhauer

Tubular disorders in childhood are predominantly of genetic aetiopathology. Yet, genetic testing has been a challenge due to the large number of genes involved. The EU FP7 grant EURenOMICS provided kits for multiplex PCR (designed by Multiplicom) of 37 genes involved in renal tubulopathies. Individual patient samples were amplified with “barcoded” primers and analysed by next generation sequencing. We here provide our experience from the first 100 samples.

The key points would be:

- The Multiplicom panel reliably detects mutations in tubulopathy genes
- The mutation detection rate is very high in patients with well characterised phenotype
- The absence of mutations in known genes in some patients with a well characterised phenotype suggests the existence of additional disease genes
- Mutation identification informs patient management and genetic counselling.
Communications orales

Oral presentations
**OP1: Pre-emptive kidney transplantation is associated with improved graft survival in children: data from the French renal replacement therapy registry**

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**Introduction:** Kidney transplantation (KT) is the treatment of choice for end-stage renal disease. Preemptive KT is considered to be the most optimal treatment of ESRD particularly in children but reports on the results of pediatric preemptive KT are scarce. The objective of this study was to evaluate the impact of preemptive KT on the risk of graft failure in children with ESRD.

**Methods:** We analyzed all first kidney transplants performed in children <19 years in France between 1994 and 2012. A Cox multivariable model with competing risk analysis was used to study the impact of preemptive KT on the hazard of graft failure defined as return to dialysis, retransplant, or death, whichever occurred first.

**Results:** A total of 1920 pediatric patients were included, of whom 387 (20.2%) received a preemptive KT. Median time of follow-up was 7.0 years (IQR 3.0-11.7). At 10 years post transplant, graft survival was 85.2% in preemptive KT and 67.1% in non-preemptive KT (p<0.001). After adjustment for recipient age and sex, primary kidney disease, donor type (living or deceased donor), donor age, HLA mismatches, and cold ischemia time, and year of KT, preemptive KT was associated with a 45% reduction in the hazard of graft failure when compared with dialysis prior to KT (HR 0.55; 95%CI 0.41-0.73; p<0.001). Patient survival was not significantly influenced by preemptive KT. The impact of preemptive KT on graft failure risk was greater among deceased donor transplant recipients (HR 0.52; 95%CI 0.37-0.72) than in living donor kidney recipients (HR 0.67; 95% 0.31-1.25). Pretransplant dialysis was associated with an increased hazard of graft failure, whatever the duration of dialysis.

**Conclusion:** In France, preemptive KT in children is associated with a lower risk of graft failure than KT performed after the initiation of dialysis, and should be encouraged when feasible.
OP2: Cytomegalovirus prophylaxis after kidney transplantation in children: longer is better

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Background: CMV infection is the second most frequent opportunistic infection following kidney transplantation. Moreover, CMV infection and CMV disease are known as independent risk factors for acute rejection, and CMV viremia can lead to chronic allograft injury and subsequent graft failure. Conducted in 2010, the IMPACT study showed that extending valganciclovir prophylaxis from 100 to 200 days significantly decreased CMV disease in adult kidney transplant recipients. However, CMV prophylaxis has never been specifically codified in pediatric kidney transplant recipients.

Methods: this monocentric retrospective cohort study compared the efficacy and safety of 100-day versus 200-day CMV prophylaxis in 64 pediatric kidney transplant recipients between 2005 and 2015, at one-year post-transplantation. Main outcomes included CMV disease and infection, rejection, eGFR, graft loss and treatment tolerance.

Results: CMV infection or disease were significantly lower in the 200-day group (23% versus 52%, p = 0.026 at one year). There was no significant difference in the GFR between groups. Treatment was well tolerated (12% of prophylaxis stopped, side effects were reversible). Longer prophylaxis was not associated with an increase of adverse effects. 100-day prophylaxis and living donor were the only significant risk factors found in multiple variable analysis (respectively OR = 9.1, 95% CI 1.61-58.5 and OR = 14.89, 95% CI 2.04-108.46).

Conclusion: 200-day compared to 100-day prophylaxis safely reduces CMV infection or disease at one-year post-transplantation in pediatric kidney transplant recipients. Living donor was the highest independent risk factor in multiple variable analysis. These results also suggest that a longer prophylaxis, if well tolerated, could decrease CMV infection and CMV disease even further in pediatric kidney transplant recipients.

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Introduction: Post-transplant infection-related hospitalizations have increased over time in children after renal transplantation. We attempt to describe those hospitalizations in a cohort of pediatric renal transplant recipients, to study the risk factors of infections and to evaluate the additional cost of those hospitalizations.

Material and Methods: Patients under 20 years receiving a kidney transplant in France between 2008 and 2013 were screened from the National medico-administrative Hospital Discharge database and a probabilistic matching was performed with the National Renal Transplant Database. Costs’ calculation was based on the Public Health Care Tariff. We used Cox regression to study the risk factors of hospitalization. To assess the evolution of the risk with time, we calculated the instantaneous risk of hospitalization per month for all infections and by type of infection.

Results: Among 593 patients, 660 hospitalizations in 260 patients were identified; median follow-up time was 34.7[14.7-53.2] months. The first cause of hospitalization was UTI, incidence rate of 16.6 per 100 patient-years (py) followed by viral infections (15.6/100py) including 128 digestive infections, 70 respiratory tract infections and 47 hospitalizations related to herpes viruses. Risk factors of hospitalization were a younger age (HR 0.95 [0.92-0.97] per year), HLA mismatches (HR 1.14[1.01-1.28] per mismatch) and the use of Cyclosporine rather than Tacrolimus (HR 0.72[0.54-0.95]).

Female gender, uropathy and cold ischemia time were specific risk factors of UTI. Instantaneous risk of infection decreased with time but CMV infection displayed a peak at the end of the prophylaxis. Total cost of infection-related hospitalizations was 1600k€ (933€/py) for 3529 days of hospitalization.

Conclusion: This study points out the high burden of infection in pediatric transplanted patients, especially the youngest ones in terms of quality-of-life and health cost and highlights possible ways of improvement for clinical practice.
Introduction: Donor-recipient HLA mismatch is widely assessed with the number of HLA antigenic mismatches between donor and recipient. However, the epitope load, i.e. the number of epitope mismatches, seems to be more informative. We ought to evaluate the capacity of epitope load to predict development of Donor Specific Anti-HLA antibodies (DSA) and occurrence of antibody-mediated rejection (AMR) in a pediatric renal transplant population.

Methods: In this retrospective monocenter study, we included the 76 consecutive children who had undergone renal transplantation at Necker Children’s Hospital between 2010 and 2015, without any pre-transplant DSA. The number of HLA antigenic mismatch, the epitope load (determined with the HLA-Matchmaker software), the occurrence of de novo DSA (MFI>500) and AMR were analysed. Nonadherence and immunising events were also assessed as potential confounding factors.

Results: We observed a relationship between epitope load and development of de novo DSA. Epitope load was significantly greater in patients who developed DSA :45 mean ±16.9 vs 34 ±18.7, p=0.038)A threshold >20 Class I epitope- mismatches was associated to a relative risk of developing Class I DSA of 3.79 (CI95 [1.23-11.73]). Similarly, a global epitope load >45 conferred a relative risk of 2.18 (CI95 [1.05-3.69]) of developing Class I or II DSA. The model was not predictive for Class II only DSA occurrence, maybe due to difficulties in determining the de novo character of some class II DSA. We did not show any direct relationship between epitope load and antibody-mediated rejection, whereas there was a strong link between de novo DSA and humoral rejection as expected (p<0.001).

Conclusion: Our study shows in a pediatric population, a relationship between epitope load and de novo DSA known to impair renal allograft survival. We have also found significant epitope load thresholds allowing identification of patients at the highest risk of DSA development, for example after immunosuppression minimisation. Envisioned as a graft allocation tool, HLA epitope load, by avoiding highly immunogenic epitope- mismatches, could be a potent strategy to minimize post-transplantation immunisation, deleterious in pediatric patients.
Rituximab, the anti-CD20 monoclonal antibody, is effective in reducing relapses in nephrotic syndrome. Published series have predominantly used 1.5 g/m^2 over 2-4 doses. With the lowest effective dose to be elucidated, balancing this against potential long term side effects is important. We report our experience with a single 375 mg/m^2 dose.

We retrospectively examined notes of 20 patients with FRNS/SDNS treated over 6 years at a regional centre. 19 patients received a first dose of 375 mg/m^2; 1 patient received a second dose after 14 d.

11 patients were male. The median age at diagnosis was 3.5 y (range: 1.8-11.3). Time from diagnosis to first dose was 5.5 y (2.3-11.3). One or more renal biopsies were performed in 18 patients: minimal change disease was seen initially in all patients; calcineurin-inhibitor toxicity was seen in 9 patients prior to rituximab.

Following a first dose, 4 patients have remained in remission (median follow-up 734 d). Time to B cell depletion (<0.2 x 10^9/L) after first dose was 17.5 d (0-75). 5 patients received a prophylactic 2nd dose after 180 d (148-321). The remaining 11 patients relapsed after 272 d (149-568) and received a 2nd dose after 321 d (154-616). 12, 8 and 6 patients received a third, fourth and fifth dose respectively. Most patients received repeated doses prophylactically after a second. Median time to B cell repopulation after 1st dose was 208 d (149-479). 6-month relapse free time was 86.7% in those not given a prophylactic dose. Adverse events were few.

Our data demonstrates that a single dose of 375 mg/m^2 induces B cell depletion and maintains remission comparable to larger doses. A lower dose has cost-effective benefits but may also reduce the risk of long-term adverse effects. Further work is needed to optimise treatment strategies for repeated rituximab dosing.
Introduction. Rituximab (RTX) is an effective alternative treatment for severe idiopathic nephrotic syndrome in children. Nevertheless the actual indication of RTX within the therapeutic strategy remains controversial given the lack of data on the safety of this treatment in this setting.

Objective. To retrospectively collect and describe all severe and significant adverse effects that had occurred in children treated with RTX for idiopathic nephrotic syndrome.

Patients and methods. All participating centres within the SNP network were asked to fill an online database for all their patients treated with RTX for INS. Data were collected from the patients’ medical charts. Severe or significant adverse effects were defined as follow: any event that led to (i) a vital risk, (ii) an hospitalisation or a prolongation of hospitalisation, (iii) the occurrence of sequelae or (iv) the interruption of RTX therapy.

Results. 23 centres participated to the study. 196 cases were collected on October 10th. The mean age at diagnosis was 4.7(±3.2) years. The mean duration of disease was 7.5(±4.3) years when RTX was first used. The mean follow up was 3.2(±2.5) years and 1.5(±1.7) years since the first and the last infusion of RTX respectively. Adverse effects were reported in 6.6 % of cases during the infusion (dyspnea=6, cardiac arrhythmia=1, hemodynamic instability=1, others=7), and in 13.1% of cases after the infusion (in relation with neutropenia = 6, low IgM = 3, low IgG = 6, infectious disorder = 14, cardiac = 2, liver = 1, kidney = 1, digestive = 2, neurological = 2, others = 6, several complications can be present in the same patient). The main consequences of these adverse effects were: non-planed hospitalisations (n=30), modifications or interruptions of RTX treatment (n=6), significant invalidity (n=3). A single adverse effect led to a life threatening situation.

Conclusion. Adverse effects were reported in 18.9% of these 196 patients treated by RTX for INS. RTX treatment was interrupted or modified in 6 cases. Only 4 adverse effects led to severe consequences (either life threatening event or significant invalidity). These results will help to evaluate the benefit/risk ratio or RTX for INS in children. This is an ongoing study, therefore results can be different when they will be presented during the meeting.
**OP7:** Rituximab and intravenous immunoglobulin in the treatment of steroid-dependant nephrotic syndrome


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**Introduction:** Recent studies demonstrated the ability of Rituximab (RTX) to decrease the number of relapse in children with steroid-dependant nephrotic syndrome (SDNS). However, the remission rate after two years is only 30 to 40% and strategies using repeated RTX injections increase the risk of infection and of persistent hypogammaglobulinemia. Polyvalent Intravenous Immunoglobulin (Ivlg) demonstrated the ability to modulate B cells immune response both in vitro and in vivo. We aim to evaluate the efficacy of the association of Rituximab and Ivlg to induce long-term remission in children with SDNS.

**Material and methods:** 28 patients with SDNS were included in a pilot study and treated with 1 injection of RTX 375mg/m² followed by Ivlg 2g/kg once a month for 6 months and were compared with a historic cohort of 43 patients treated with a single injection of RTX. The primary outcome was the relapse-free survival 24 months after RTX injection. Cox regression was used to adjust for potential confounders.

**Results:** Compared to the control group, our patients were significantly younger (median age in years: at first flair 2.4 vs 4.4 and at RTX 12.0 vs 13.8, p=0.04). They also presented a shorter duration of B-cell depletion (4.0 vs 5.6 months, p=0.03. Two-years relapse-free survivals were 45% and 30% in the experimental and control group respectively with a statistically significant difference in favor of Ivlg (HR 0.32 [0.15-0.69]).

**Conclusion:** The association of Ivlg with RTX improved relapse-free survival in children with SDNS. This finding gives new insight in the pathophysiology of SDNS and offers new hypothesis for basic research. A prospective randomized trial is currently ongoing to further demonstrate the efficacy of this strategy.
OP8: Non-genetic congenital and infantile nephrotic syndrome: new diagnostic and therapeutic management.

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Introduction: 30% of congenital and infantile nephrotic syndromes (CINS) are not caused by a genetic mutation. Non-genetic CINS (NGCINS) is a poorly characterized entity. No clear guidelines can be found in terms of diagnosis, prognosis and treatment of NGCINS patients. Noteworthy, NGCINS morbidity and mortality remain high, which makes it an important issue in Pediatric Nephrology.

Material and methods: this multicentric retrospective cohort study involved 12 pediatric nephrology departments across France. 35 NGCINS patients, diagnosed between 1965 and 2015, were analyzed. Main outcomes included clinical presentation, pathology results, treatments used, relapses, survival, long term renal function and morbidity.

Results: 35 patients were analyzed.

- 6 patients had no steroid treatment; 3 had spontaneous remission; 2 had persistent proteinuria evolving to ESRD and kidney transplantation; 1 had positive CMV PCR and was successfully treated with valganciclovir.

- 29 patients were treated with steroids; - 13 were steroid-sensitive (SS) - 16 patients were primary steroid-resistant (SR); 14 received one immunosuppressive therapy, 7 remained proteinuric; 2 of the latter died and 2 other evolved to ESRD and kidney transplantation.

In sub-group analysis: - Pathology results were similar in SS and SR patients; morbidity (43% versus 0%), and mortality (3 patients versus 0) were higher in the SR group.

- Morbidity and mortality were higher in younger patients (< 3 months old), with increased ESRD (62.5%).

Conclusion: this study attempts to characterize NGCINS. The following conclusions can be drawn:

- CMV PCR should be proposed to every CINS patient; valganciclovir treatment should be used in case of a positive result.

- 30-day oral steroid treatment should be initiated early; complementary methylprednisolone IV boluses do not seem efficient.

- Renal biopsy does not provide significant diagnostic or prognostic information.

- Genetic testing should be proposed early to CINS patients.

- Intensive immunosuppressive treatments should be initiated early for SR NGCINS patients; multiple lines of treatment can be used.
OP 9: Cakutome, a high-throughput tool for molecular diagnosis and identification of novel causative genes for CAKUT patients

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Introduction: Congenital anomalies of the kidney and urinary tract (CAKUT) are a major cause of renal failure in children. CAKUT are phenotypically and genetically heterogeneous and more than 50 genes have been reported as mutated in patients. The most frequently mutated genes are those encoding transcription factors HNF1B, PAX2, EYA1 and SIX1. Most of the other genes are only mutated in a few patients and their implication is sometimes elusive.

Methods: We developed a targeted exome sequencing strategy (“CAKUTOME”, sureselect Agilent) focusing on 330 genes, including known validated or likely causative CAKUT genes, as well as candidate genes. 215 unrelated patients were analysed, including 50 who had previously been tested for HNF1B, PAX2, EYA1 and/or SIX1 mutations by Sanger sequencing.

Résultats, discussion, conclusion: This approach proved to be an efficient and cost-effective strategy to identify pathogenic mutations and copy number variations in known CAKUT genes. The 25/165 rate of mutation we identified in HNF1B, PAX2, EYA1 or SIX1 is similar to the one obtained by Sanger sequencing. In addition, we identified heterozygous mutations in ANOS1 (Kallmann syndrome), GATA3 (hypoparathyroidism, deafness and kidney disease), or CHD7 (Charge syndrome), and biallelic mutation in KIF14 in 2, 3, 1 and 2 cases, respectively. Our data also led to the identification of a novel CAKUT gene, the mutation/deletion of which affected 5 unrelated cases in the cohort. Moreover, we identified variants in several other genes never reported as mutated in CAKUT patients, whose pathogenicity is being tested. Finally, no relevant variant was identified in 40% of our series. Although mutations in gene(s), non-coding regions or microRNAs not targeted in our CAKUTOME could be involved in some of these cases, complex inheritance, somatic events, and/or environmental factors or epigenetic mechanisms likely explain this large fraction of cases.
OP10: French cohort of transient antenatal Bartter syndrome with MAGED2 mutations

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Background: MAGED2 was recently identified in an X-linked severe and transient form of antenatal Bartter’s syndrome associated with polyhydramnios and prematurity but also in idiopathic polyhydramnios in the male offspring. An inappropriate expression of the sodium-chloride transporters NKCC2 and NCC is disclosed.

Methods: MAGED2 was screened by Sanger Sequencing in a series of 35 cases with transient or antenatal Bartter’s syndrome and no pathogenic variant in SLC12A1, KCNJ1, CLCNKB and BSND genes.

Results: We found 15 cases from 14 families harboring MAGED2 variants including four nonsense, three missense, two frameshift and two splice-site variants; two small in frame deletions and one complete deletion of MAGED2 gene. Only one variant was previously reported, p.Arg446Cys. Severe polyhydramnios occurred in all pregnancies, at 18 to 25 weeks of gestation requiring serial amniocentesis (one to ten, when data available). In four cases, polyhydramnios was present in previous or later pregnancies. One pregnancy resulted in medical termination of pregnancy. All the infants (14) were born preterm with gestational age at delivery between 26 and 36 weeks. All presented a Bartter’s syndrome with severe polyuria (median diuresis was 13 mL/kg/h). Surprisingly, two cases were female. The severity of their phenotype and the course of the disease were comparable to those for male. The medical follow-up of 12 patients revealed that the salt and water losses resolved between 2 and 18 months with the end of indomethacin treatment or water and salts supplements. Two cases, with associated neurological disorders died at 1 and 12 months.

Conclusion: We confirmed with our French series of 15 MAGED2 cases the phenotypic presentation of this transient antenatal Bartter’s syndrome. This new syndrome has to be considered in the differential diagnosis of Bartter’s syndrome with the screening of MAGED2 as part of the molecular diagnosis.
Background

Bartter and Gitelman syndrome are rare autosomal recessive disorders of renal salt handling. They are characterised by disturbed electrolyte and acid-base homoeostasis with potentially severe complications. Currently little is known about the long-term disease course and best treatment is controversial.

We performed a retrospective case review to investigate the long-term disease course of patients with Bartter and Gitelman syndrome.

Methods

Demographic and Laboratory data was recorded at presentation, and ages 1, 2, 3, 4, 5, 10 and 15.

42 patients with a genetic diagnosis of Bartter/Gitelman were reviewed with a median follow up of 7.85 years (Range 0-18 Years).

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Number of patients</th>
<th>Age at Presentation</th>
<th>Gestational Age</th>
<th>Nephrocalcinosis (% of patients)</th>
<th>GFR &lt;90ml/min/1.73m² at last follow-up (Schwartz)</th>
<th>Average Height at last follow-up (Z-score)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bartter</td>
<td>1</td>
<td>Day 7</td>
<td>30.3</td>
<td>100</td>
<td>6</td>
<td>-1.2</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.8 Years</td>
<td>32.0</td>
<td>70</td>
<td>9</td>
<td>-1.82</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>2.7 Years</td>
<td>37.4</td>
<td>7</td>
<td>4</td>
<td>-1.28</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Day 1</td>
<td>32.0</td>
<td>0</td>
<td>1</td>
<td>N/A</td>
</tr>
<tr>
<td>Gitelman</td>
<td>11</td>
<td>5 Years</td>
<td>39.4</td>
<td>9</td>
<td>1</td>
<td>-0.93</td>
</tr>
</tbody>
</table>
Results

Bartter 1&2 presented earliest with prematurity and deranged electrolytes. All of the Bartter 1 patients and 70% of Bartter 2 had evidence of nephrocalcinosis on their first ultrasound.

Hypomagnesaemia (<0.7mmol/L) was seen in 11/14 Bartter 3 and 8/11 Gitelman patients; Hypomagnesaemia developed over time and was seen earlier in Bartter 3 (3.8 years) than in Gitelman (7.9 years).

Obvious complications of hypokalaemia were only seen in one patient with Bartter 3 (despite potassium levels <2.5mmol/L in 10 patients) in the form of hypokalaemic paralysis; he was admitted twice at age 2 and 3 (Potassium 1.7 & 1.5 respectively). Decreased GFR was present in all Bartter 1 and 90% of Bartter 2 at last follow-up 3 patients with Bartter 3 developed nephrotic range proteinuria with one patient demonstrated biopsy evidence of FSGS.

Discussion & Conclusion

The overall prognosis during childhood was good for these disorders. Final height was within the normal range and no child developed ESRD. Decreased GFR was common in this cohort, indicating the need for long-term monitoring of renal function. Interestingly, hypomagnesaemia is often absent at presentation and develops over time in both Bartter 3 and Gitelman.
OP12: Autologous Arteriovenous Fistulae using microsurgery for hemodialysis in young children weighing 20kg or less: Single center experience.

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Introduction: Arteriovenous autologous fistula (AVF) is the best vascular access (VA) for hemodialysis but its feasibility in smaller children remains a surgical challenge. This study aims to describe a single-center experience regarding the efficiency, longevity and associated morbidities of AVF created in children weighting ≤ 20 kg.

Material and Methods: We collected data of all AVF created using microsurgery techniques after preoperative ultrasound vascular mapping between 1988 and 2011. Primary patency (PP) was defined as the interval time from VA creation until any intervention designed to maintain or reestablish patency or until VA abandonment (failure or transplantation). Secondary patency (SP) was defined as the interval time from creation to VA abandonment.

Results: 50 AVF (36 distal, 14 proximal) were created in 40 children with a median weight of 13 kg (range 6 to 22). 22 children were already on extra-renal epuration: 18 on HD via central venous catheter and 4 on peritoneal dialysis. Early complications during the first month after AVF creation were observed in 8 AVF, 6 thrombosis which were abandoned and 2 non maturations (1 re-operated successfully). Median time to maturation (first utilization in HD) was 4 months. Secondary complications observed between the first month after AVF creation and transplantation or VA failure were the following: 18 thrombosis (39% of which occurred during transplantation surgery), 22 stenosis (15 corrected by angioplasty, 4 by surgery whether 3 ended to AVF failure) and 3 high blood flow rate (1600, 1850, 2100 mL/min/1.73 m²) without evidence of cardiac complications. Median duration of PP and SP were 7 and 17 months respectively.

Conclusions: In our experience, AVF is feasible in younger children with 86% of success. Time to maturation is longer than in older children but SP after creation is excellent. Attention should be paid during transplantation surgery, as thrombosis rate is considerably high.
Background: The precise incidence of acute kidney injury (AKI) in the paediatric age group is unknown, partly due to the lack of a universally agreed definition in the past. We conducted this study to assess incidence of AKI among hospitalised children on World Kidney Day 2016.

Methods: Cross-sectional study involving 8 tertiary paediatric centres across England, Scotland, Wales and Northern Ireland. Centres reported numbers of new cases of AKI on a single observation day, associated clinical features and follow-up data where available. Cases were defined according to the KDIGO (Kidney Disease: Improving Global Outcomes) AKI definition.

Results: On the observation day, there were 1218 inpatients in 8 centres. 31 children (2.5%) met the case definition for AKI. The majority of patients had no pre-existing, known risk factors for AKI (20/31, 65%), while the leading known risk factor was congenital heart disease (5/31, 15%). Most cases of AKI were hospital acquired (25/31, 81%). The leading contributory factors were: medications (13/31, 42%), hypotension/shock (10/31, 32%) and dehydration (10/31, 32%). AKI was subdivided according to severity: stage 1 (25/31, 81%), stage 2 (2/31, 6%) and stage 3 (4/31, 13%). Follow-up results at 7 days were available for all 31 cases. Renal replacement therapy was required in 2 cases (6%). Recovery from AKI at 7 days was: complete (18/31, 58%), incomplete (9/31, 29%) or unknown (4/31, 13%); 2 patients (6%) died from non-renal causes.

Discussion & Conclusion: This is the first study looking at the point incidence of AKI in hospitalised paediatric patients according to the KDIGO AKI classification. Our estimated point incidence of 2.5% is similar to international reports. The majority of cases were hospital acquired and the leading contributory factor was nephrotoxic medication, a significant modifiable factor. Further prospective studies will be necessary to evaluate the benefit of interventions designed to reduce the incidence of AKI in paediatrics.
OP14 : Time to STOP Acute Kidney Injury (AKI)

Amanda Newnham, Dr Kay Tyerman

Paediatric Nephrology Leeds Children’s Hospital, UK

Background:
Acute kidney injury (AKI) is a serious condition that is often unrecognised leading to delays in treatment. AKI has is an independent risk factor for mortality, intensive care admission and length of stay in hospital. In the UK a National Patient Safety Alert was issued around the recognition and response to AKI as a preventable cause of death and an estimated annual cost of £500 million per year to the NHS. A UK BAPN audit in 2012 of 6 centers showed >60% of AKI cases were unrecognised. Studies in adults on electronic alerts (e-alerts) for AKI have shown an improvement in recognition but not subsequent response with fluid resuscitation and timely antibiotics.

Method:
A Quality Improvement Project was devised in a large tertiary children’s hospital in the UK to improve response and recognition to AKI. The project was based on the children’s oncology unit which is an area of high incidence of AKI with high risk patients, often in high risk scenarios. The project utilised Plan Do Study Act (PDSA) cycles and the improvement model. The stages are: initiation of e-alerts on the blood results server, raising awareness of e-alerts, education package on AKI response and recognition which is now informing the development of a AKI care bundle.

Results:
The overall incidence of AKI is low, mean 8-10 per week since the interventions there has been an increase in recognition and a decrease in the number of AKI stage 1 that progressed. There has been no increase in the number of blood tests being requested (balancing measure). Interestingly false positive alerts have been seen in children on hyperhydration for risk of tumour lysis syndrome.

Conclusion: A multidisciplinary approach can achieve improvements in recognition & response to AKI.
Background and aims: Reporting estimated glomerular filtration rate (eGFR) is established adult practice. eGFR formula in children commonly require height which is not routinely available. We report optimisation and validation of a height-independent eGFR formula, biochemistry reporting of this formula and the impact of reporting eGFR on nephrology referrals.

Methods: 117 paediatric patients (60 male, mean age 10.5 years) who underwent a nuclear medicine GFR (mGFR) from April 2013 until October 2014 in Nottingham Children’s Hospital(NCH) were identified. eGFR was calculated using published formula. The Solver function of Excel to minimise the sum of the squares of the differences between the eGFR and mGFR was used to locally optimise the formula (table 1). Validation consisted of 90 paediatric patients (55 male, mean age 7.7 years) who underwent a mGFR in Sheffield Children’s Hospital(SCH) between January 2012 and September 2015.

The NCH biochemistry reporting system was programmed to report eGFR. Manually calculated eGFR in 20 patients (13 male, median age 9.6 years) were compared to the reported eGFR. We collected data on referrals before and after the introduction of eGFR reporting on 10th March 2016.

Results: The accuracy of each formula was assessed and compared to two commonly used adult formula (table 2). The biochemistry reporting system was accurate (Figure 1). Following introduction of the automated report there was an increase in telephone referrals and requests for renal ultrasound. One patient was identified with renal scarring.

Conclusions: Automated reporting of eGFR is feasible in children. We are reporting eGFR in all hospitalised children age 2 to 16 years of age whenever a serum creatinine is checked. This has not previously been described in paediatrics. This has been shown to lead to earlier identification of patients with CKD in adult services and should now become a standard of care in paediatric services.
**Table 1: Formula used to calculate eGFR**

<table>
<thead>
<tr>
<th>Formula</th>
<th>Formula Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard Schwartz formula</td>
<td>$= 40 \times \text{height (cm)} / \text{SCr (\text{\textmu}mol/l)}$</td>
</tr>
</tbody>
</table>
| NCH Schwartz formula                 | $= k \times \text{height (cm)} / \text{SCr (\text{\textmu}mol/l)}$  
  Where $k = 36$ in males 13 years of age or older  
  and $k = 30$ in all other cases |
| SCH Schwartz formula                 | $= k \times \text{height (cm)} / \text{SCr (\text{\textmu}mol/l)}$  
  Where $k = 27$                            |
| Height independent formula (BCCH2)   | $= \text{Inverse ln of: } 8.067 + [1.034 \times \text{ln(1/SCr (\text{\textmu}mol/l)})] + (0.505 \times \text{ln(age years)}) + 0.054$ if male |
| Modified height independent formula (NCH-NCCH2) | $= \text{Inverse ln of: } 6.064 + [0.554 \times \text{ln(1/SCr (\text{\textmu}mol/l)})] + (0.254 \times \text{ln(age years)}) + 0.025$ if male |

**Table 2; Analysis of eGFR formula with mGFR as standard**

<table>
<thead>
<tr>
<th>Mean difference</th>
<th>S.D.</th>
<th>R (Correlation)</th>
<th>% Diff &lt; 20%</th>
<th>% Diff &lt; 30%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard Schwartz</td>
<td>30.5</td>
<td>51.0</td>
<td>0.668</td>
<td>35%</td>
</tr>
<tr>
<td>NCH Schwartz</td>
<td>16.8</td>
<td>17.2</td>
<td>0.695</td>
<td>63%</td>
</tr>
<tr>
<td>SCH Schwartz</td>
<td>21.7</td>
<td>21.23</td>
<td>0.516</td>
<td>66%</td>
</tr>
<tr>
<td>BCCH2</td>
<td>34.5</td>
<td>35.1</td>
<td>0.659</td>
<td>34%</td>
</tr>
<tr>
<td>NCH – BCCH2 - Derivation</td>
<td>11.6</td>
<td>9.4</td>
<td>0.745</td>
<td>76%</td>
</tr>
<tr>
<td>NCH – BCCH2 - Validation</td>
<td>15.8</td>
<td>12.7</td>
<td>0.60</td>
<td>72%</td>
</tr>
<tr>
<td>EPI-CKD</td>
<td></td>
<td></td>
<td></td>
<td>83%</td>
</tr>
<tr>
<td>MODD</td>
<td></td>
<td></td>
<td></td>
<td>81%</td>
</tr>
</tbody>
</table>

![Figure 1 - Correlation of calculated and reported eGFR](image)
OP16: Effect of Nonsteroidal Anti-inflammatory Drugs in Children with Bartter syndrome.

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Introduction: Bartter syndrome (BS) is a congenital salt-wasting tubulopathy with an induced expression of cyclooxygenase-2 in the macula densa leading to hyperreninemia. Renin Angiotensin Aldosterone system (RAAs) activation leads to hypokalaemic alkalosis. NSAIDs are now currently used in BS, however few studies have investigated the effect of NAIDs on RAAs activation, biological parameters and treatment modifications.

Material and methods: We included 19 patients with BS treated with NAIDs between 1994 and 2016. We assessed renin and aldosterone serum levels, serum electrolytes, calcium, phosphorus, Vitamin D and PTH before and after treatment initiation. We also recorded modifications in sodium and potassium supplements and adverse events.

Results: Median age and weight at treatment initiation were 7 [4-49] months and 6175 [4360-13675] grams respectively. Serum renin and aldosterone levels significantly decreased from 1532 [952-2638] to 226 [132-704] pg/mL (p<0.001) and from 380 [206-1100] to 229 [64-301] ng/mL (p=0.02) respectively. There was a trend towards an increased kalaemia (2.9 [2.4-3.5] to 3.3 [2.9-3.9], p=0.17). NSAIDs allowed a major reduction of oral sodium supplements from 10.8 [5.4-14] to 6.3 [2-10.1] mEq/kg/day and from 3.8 [1.7-9.0] to 1.7 [0.5-5.2] mEq/kg/day of potassium (p<0.001). We also found a significant decrease of the calciuria from 3.9 [1.5-4.8] to 1.2 [0.2-2.4] mmol/mmol of creatininuria (p=0.02). Nine patients presented a high serum PTH level among whom eight completely normalized after treatment without any modification of the vitamin D and calcium supplements. Four patients presented gastro-intestinal complications.

Conclusion: In this report we confirm the major benefit of NSAIDs treatment in patients with BS. We also assess that monitoring renin serum level is of interest to adapt patients’ treatments. Finally, we demonstrate a beneficial effect of NSAIDs both on the decrease of the calciuria and the decrease of bone turn-over.
OP17: Inter-observer variability of the histological classification of lupus glomerulonephritis in children

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Background. The gold standard for the classification of lupus nephritis (LN) is based on renal histology but variation in interpretation exists. The aim of this multicentre international study was to assess the inter-observer variability of the 2003 International Society Nephrology/Royal Pathology Society (ISN/RPS) LN histological classification criteria in children.

Methods. Expert histopathologists from a reference centre (USA) and three tertiary pediatric centres (UK) independently scored digitalized histology slides from percutaneous kidney biopsies of 55 children with LN. Histological ISN/RPS Class and additional features (LN-activity [scored 0-24], LN-chronicity [0-12], and tubulointerstitial activity (TIA) [0-21]) were scored. Statistical analysis (Kappa score and intra-class correlation, ICC) quantified the level of agreement, interpreted as: 0.01-0.20 slight; 0.21-0.40 fair; 0.41-0.60 moderate; 0.61-0.80 good; 0.81-1.00 excellent agreement.

Results. In the cohort (73% females) the mean ± standard error (SE) age at the time of biopsy was 15.5±0.39 years. Based on the reference centre, 42% (23/55) had ISN/RPS Class IV with a LN-activity score of 4.23±0.50, LN-chronicity 1.81±0.18, and TIA 4.45±0.35. There were between 4-54 (mean 16.7) glomeruli per biopsy. Pathologists had only fair agreement for LN ISN/RPS assignment (kappa 0.26±0.12). LN-chronicity and TIA scoring were also only fair (ICC 0.36±0.09 and 0.22±0.09 respectively). Conversely, there was good agreement for scoring LN-activity features (ICC 0.69±0.06). When the biopsy findings were categorized into proliferative and non-proliferative disease, poor agreement remained (kappa 0.24±0.11).

Conclusion. Despite unified criteria for the interpretation of histological features of LN, marked reporting variation remains and this may influence treatment decisions. Adding activity features to the biopsy report improves inter-observer agreement. Supplementary measures of predicting the extent of LN, such as the use of non-invasive urine biomarkers, are required.
OP 18: Mycophenolic acid area under the curve is associated with therapeutic response in pediatric lupus nephritis

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**Introduction:** Mycophenolic acid (MPA), the active metabolite of mycophenolate mofetil (MMF), is an effective treatment in lupus nephritis. Therapeutic drug monitoring studies of MMF suggest that area under the concentration-time curve (AUC) values of MPA of 30-45 mg.h/L may be associated with better outcome in adults with lupus but data in children is scarce.

**Methods:** In this retrospective study, 27 children were treated with MMF for biopsy proven class III-IV-V lupus nephritis between 2009 and 2016. AUC of MPA was determined on the basis of sampling times at 20, 60, and 180 minutes postdose using a Bayesian estimator. In 25 children, AUC was performed within 6 months after kidney biopsy and MMF initiation. Treatment response at 6 months of MMF treatment was defined as follows: normal or improved GFR by 25% compared to baseline, 50% reduction of proteinuria resulting in a level <0.5 g/day or 50 mg/mmol, no hematuria defined as red blood cells <10000/ml or ≤1+ by dipstick testing.

**Results:** In total, 62 AUC of MPA were analyzed (median 44 mg.h/L [IQR 33-54]) in 27 patients. The findings indicate individual dose adaptation in 32 cases (52%) to achieve an AUC target of 30-60 mg.h/L. At 6 months, 14/25 patients were defined as responders (56%) with a median AUC value of 49 [40-59] and 11/25 as non-responders (44%) with a median AUC value of 29 [24-38]. Patients with MPA AUC levels of >45, 30-45, and <30 had response rates of 89% (8/9), 60% (6/10) and 0% (0/6) at 6 months. In a multivariable logistic regression model adjusted for age, sex, disease classification and time since MMF, an AUC >45 was significantly associated with therapeutic response (OR 3.9, CI95% 2.4-10.5, p<0.03).

**Conclusion:** Therapeutic drug monitoring leading to individualized dosing may improve the efficacy of MMF. An AUC of MPA >45 mg.h/L is associated with a better response rate and may be considered as a target value in pediatric lupus nephritis.
OP19 : Outcome following switch between Brand Name and Generic Tacrolimus in Paediatric Population

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² Peter Foxon, Senior Clinical Pharmacist, Nottingham University Hospitals NHS Trust
³ Dr. Martin Christian, Consultant Paediatric Nephrologist, Nottingham University Hospitals NHS Trust

Introduction

For many medicines a switch between formulations can be done with little monitoring. Tacrolimus provides an interesting challenge due to its narrow therapeutic window requiring careful medical supervision and therapeutic monitoring. Currently, there is limited evidence to show the effects of a switch between Tacrolimus formulations in paediatric patients. We present the effects of our study switching our patients from brand to generic formulation.

Method

Patients were given written and verbal advice to switch from Prograf® to the same dose of Adoport® two weeks before their next clinical review and bloods were tested. Then, we reviewed the data for Tacrolimus and Creatinine levels before and after the switch and assessed for any clinical variation.

Results

41 stable patients were switched from Prograf® to Adoport®. 4 patients were lost to tertiary follow up. 6 patients had a rise in Creatinine more than 15%; in 2 patients the rise was associated with UTI, 2 patients were treated empirically with high dose steroids for concerns of rejection, 1 patient developed swelling of legs [cause unidentified, DVT ruled out with scan] managed with increase in maintenance dose steroids and the cause was unclear in the last patient. In remaining 31 patients, there was no significant change noted in the Creatinine levels [ttest -2.38, pvalue 0.01]. One patient developed hair loss and requested to go back onto Prograf®, but all others continued on Adoport® and patients with initial rise in Creatinine stabilized to baseline.

Conclusion

This study assessed the clinical outcomes for paediatric renal transplant/nephrotic patients switching from Prograf® to Adoport®. The majority of patients tolerated the switch well. There was significant cost saving associated for NHS England of approximately £36,000 (2015-2016). Our outcome data therefore support the switch from Prograf® to Adoport® and its continued use as a potentially safe and cost-saving measure.

A Bertholet 1, C Guittet 2

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2 Advicienne

Background: Several conditions require treatment with alkalinising agents. The objective is to restore the homeostasis on various parameters or stabilise some urine parameters. The agents used currently have to be administered several times a day in order to maintain the effect but have a bad gastro-intestinal tolerability, both leading to bad compliance. A new formulation in the form of granules (ADV7103) has been developed to limit the administration to 2 intakes daily and improve gastro-intestinal tolerability.

Methods: A randomised, placebo-controlled, double-blind, two-period cross-over study has been conducted to evaluate the pharmacodynamics, safety and tolerability of repeated oral doses of ADV7103 at three dose levels, in 8 subjects. The effect was evaluated on urine pH on the first morning urines and on 12 fresh urine collections of 2 hours for 24 hours, after 4 and 5 days of treatment. The safety and tolerability was evaluated.

Results: Urine pH increased proportionally to the dose administered (Figure 1). All doses administered demonstrated a statistically significant increase of urine pH as compared to placebo (p<0.05 or p<0.0001). No saturating effect occurred within the dose-range tested.

Figure 1: Mean (±SE) urine pH profiles over time per treatment (Day 4)
A single gastro-intestinal adverse event was reported for 240 administrations: an episode of nausea of mild intensity, 30 minutes after the high dose intake. Very few urine samples were noted above pH 8.

**Discussion**

A stable urine pH over 24 hours with two doses per day was obtained for the majority of samples, despite a strong nyctohemeral rhythm.

**Conclusions**

ADV7103, proved its efficacy in maintaining a constant increase of the urine pH over 24 hours with 2 daily intakes. The safety profile has been confirmed.
POSTERS
**P1 : Renal blood flow measurements by magnetic resonance imaging using arterial spin labelling as a novel non-invasive biomarker in paediatric renal transplant recipients**

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**Objectives**: To investigate our hypothesis that non-invasive cortical renal blood flow (cRBF) measurements using functional magnetic resonance imaging (MRI) arterial spin labelling (ASL) are sensitive biomarkers of early damage of the transplanted kidney in paediatric renal transplant recipients (pRTR).

**Methods**: Prospective study of pRTR undergoing MRI imaging using 1.5T Siemens Avanto system with multi-TI pulsed ASL acquisition performed at 10-20 days, 2 and 12 months with a FAIR labelling scheme and multi-shot 3D grase imaging module with background suppression.

**Results**: 14 pRTR (50% (7) male) aged 9.2-17.1 (median 13.2) years of whom 64% (9) had ESKD due to CAKUT underwent MRI ASL after transplantation (86% (12) living-related) with eGFR of 41.0-92.0 (median 60.9) mls/min/1.73m² at follow-up of 3.5-5.4 (median 4.5) years. 46% (6) were pre-emptive transplants with 7% (1) re-transplanted. Patients had 0-5 (median 1) post-transplant UTI with 50% (7) EBV viraemia and underwent 1-7 (median 2) percutaneous renal transplant biopsies with evidence of steroid-resistant acute rejection episode due to non-adherence and borderline rejection in 7% (1) and 14% (2) pRTR respectively. Baseline MRI ASL at median 10 days showed cRBF of 86-268 (median 198) mls/100g/min with changes at subsequent and latest MRI performed at median 70 and 344 days respectively of -70 to +121 (median 52) and -56 to +147 (median 36) mls/100g/min respectively.

**Conclusions**: Renal blood flow maximises in the first month after renal transplantation with subsequent reduction in first year in pRTR. There are multiple causes of renal allograft dysfunction in pRTR and associated risks in performing surveillance percutaneous renal transplant biopsies. MRI ASL is a useful and novel non-invasive biomarker of renal allograft function in pRTR.

**P2 : Devenir à long terme des transplantés rénaux à l'âge pédiatrique : expérience d'un centre.**

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**Introduction**: Kidney transplantation is the treatment of end stage renal failure in children (ESRD). The current problem of the ESRD is not patient survival but the quality of life of transplant recipients. One of the challenges of pediatric renal transplantation is also to study long-term outcome after of transplants. Few studies report more than 20
years of follow-up. In this context, we analyzed the evolution of pediatric renal transplants performed in our single center (CHU Timone-Enfants).

**Methods:** We analyzed 146 pediatric renal transplantations performed between 1974 and 2013. We compared the cohort before 1994 (group 1, 42 grafts), to the 1994-2003‘one (group 2, 45 grafts) and the 2004-2013‘one (group 3, 59 grafts). Patient survival and graft survival at 1, 5, 10, 15 and 20 years were studied and the characteristics of the rejection, the occurrence of lymphomas and education and social outcome.

**Results:** The patient survival is at 1, 5, 10 and 20 years of 96%, 93.8%, 91.8% and 90%. No deaths found in group 3. The patient survival is significantly different between group 1 and group 2 and 3. The graft survival is at 1, 5, 10, 15 and 20 years of 90.7%, 80.1%, 70.2%, 64.8% and 56.7%. The graft survival is at 1 year in group 1, 2 and 3 respectively of 83%, 91% and 95% and at 5 years respectively of 61,6%, 86,7% et 86%. 44% of grafts will experience at least one rejection. Six lymphomas (4%) are observed. 67% of children in groups 2 and 3 have a normal education. 61% of adults late in the monitoring of groups 2 and 3 have a employment or training.

**Conclusion:** The long-term outcome of our cohort is well compared to what is described in the literature. Nevertheless, improving graft survival remains very long term a challenge.

**P3 : Impact of the transition consultation in renal transplantation**

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**Introduction:** Kidney transplantation is the treatment of choice for end stage renal disease. 80% of transplanted children reach adulthood with a functioning graft. Since therapeutic adherence and therefore renal graft survival are altered during adolescence, the transfer of these patients in adult care carries an increased risk of graft dysfunction. The transfer is defined as moment of switch from paediatrician to the adult medicine specialist. The transition is a program designed to prepare patients to transfer.

**Methods:** The aim of our study is to evaluate the impact of a transition process for Children with renal transplantation in Timone’s childrens Hospital in Marseille. We studied two cohorts of patients: one before and one after the establishment of the transitional consultation (TC). Our main objective was to assess the impact of the TC on biopsy proven acute rejection. Secondary endpoints are reduction in glomerular filtration rate (GFR) two years after the transfer, knowledge of the treatment and creatinine levels. We were also interested in searching for more subjective criteria such as the satisfaction of the transfer and the transition process.

**Results:** Both groups of patients are comparable. The TC has no impact on the frequency of acute rejection nor on GFR decrease (two years after), knowledge of treatment or creatinine levels. Satisfaction of patients about transfer are similar between the two groups. However, patients who followed the TC say they were better prepared for the transfer, but the difference is not significant (68.8% against 40%, p = 0.11).
Conclusion: In this work the TC does not affect the outcome of grafts or patients. The evaluation of our practices raises the question of its maintenance or an improvement of the transition program.

P3 : Impact de la consultation de transition en transplantation rénale

Introduction: La transplantation rénale est le traitement de choix de l’insuffisance rénale chronique terminale. 80% des jeunes adultes transplantés rénaux atteignent la majorité civile avec un greffon fonctionnel. L’adhésion thérapeutique et la survie du greffon rénal sont altérées pendant l’adolescence. Le transfert de ces patients en médecine adulte est un facteur de risque de perte du greffon. Le transfert est défini comme le changement de médecin. La transition est un programme destiné à préparer les patients au transfert.

Méthodes: Le but de notre travail est d’évaluer l’impact d’une consultation de transition (CT) en transplantation rénale au CHU de La Timone Enfants à Marseille. Nous avons étudié deux cohortes de patients : l’une avant et l’autre après la mise en place de la CT. Notre objectif principal est d’évaluer l’impact de la CT sur un critère objectif : le rejet aigu histologique. Les critères secondaires sont la diminution du débit de filtration glomérulaire (DFG) deux ans après le transfert, la connaissance du traitement et du taux de créatinine. Nous nous sommes également intéressés à des critères plus subjectifs comme la satisfaction des patients à propos du transfert et du processus de transition.

Résultats: Les deux groupes de patients sont démographiquement comparables. La CT n’a pas d’impact sur la fréquence des rejets aigus ou sur la diminution du DFG deux ans après le transfert. La connaissance du traitement et du taux de créatinine sont similaires entre les deux groupes. Les patients se disent autant satisfaits. En revanche les patients qui ont bénéficié de la CT se déclarent mieux préparés au transfert, mais la différence n’est pas significative (68.8% contre 40%, p=0.11).

Conclusion: Dans ce travail, la CT ne modifie pas le devenir des patients. L’évaluation de notre pratique soulève la question de son maintien ou de l’amélioration du programme de transition.

P4 : Quality of life after pediatric renal transplantation

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Introduction: Improvements of treatment in pediatric organ transplantation lead to consider currently the quality of life (QOL) as a challenge. However there are few studies of QOL. The objective of this study was to evaluate the QOL in pediatric recipients of a renal, heart or liver transplant, and the QOL of their parents and to identify influencing factors.

Methods: Patients Under 18-year-old who had received a renal, liver or heart transplant during the last 10 years were included. The QOL of the children and their parents were evaluated with the questionnaires adapted to children (Vécu et Santé
Perçue de l'Adolescent: Health perceived by the teenagers) and to their parents (WHOQOL). Parameters were studied in univariate analysis.

**Results**: 59 children were included, 45 completed the questionnaires. The QOL of the children was lower than the general population, except for «the general feeling» (73.4/100 vs 68.5/100) and the «vitality» (83.2/100 vs 81.4/100) and was lower than children with leukemia except for «vitality» (83.2/100 vs 81.6/100). Transplanted teenagers had QOL scores higher than the general population and than children with leukemia except for «leisures» (56.9/100 vs 62.2/100) and «psychological well-being» (72.6/100 vs 74.8/100). With hetero-evaluation, transplanted children and teenagers had higher QOL scores than the leukemia group, except for «school work», «friendly relations» and «leisures». Parents had lower scores than the general population. Children gender was not a predictive factor, in contrast to immunosuppressive treatments, parental educational level and siblings.

**Conclusion**: QOL in pediatric recipients seems to be satisfactory but the parents QOL is lower than the one of the general population.

**P4 : Qualité de vie en transplantation rénale pédiatrique**

**Introduction**: L'amélioration des traitements en transplantation d'organe solide pédiatrique permet aujourd'hui de considérer la qualité de vie comme un des éléments primordial à évaluer. Elle reste peu étudiée. L'objectif était d'évaluer la QDV des enfants transplantés rénaux, hépatiques ou cardiaques ainsi que celles de leurs parents puis de rechercher des facteurs influençant.

**Méthodologie**: Nous avons inclus des patients de moins de 18 ans ayant bénéficié d'une transplantation rénale, hépatique ou cardiaque depuis moins de 10 ans. La QDV des enfants et adolescents était évaluée à l'aide de questionnaires Vécu et Santé Perçue de l'Adolescent, adaptés à l'âge et celle des parents grâce au questionnaire WHOQOL. Les facteurs étaient analysés en univarié.

**Résultats**: Sur 59 patients inclus, 45 ont répondu aux questionnaires. La QDV des enfants était inférieure à celle de la population saine sauf pour le "bien-être général" (73.4/100 versus 68.5/100) et la "vitalité" (83.2/100 versus 81.4/100) et à celle du groupe leucémie sauf pour la "vitalité" (83.2/100 versus 81.6/100). Les adolescents transplantés avaient des scores de QDV plus élevés que ceux de la population saine et ceux du groupe leucémie sauf pour les "loisirs" (56.9/100 versus 62.2/100) et le "bien-être psychologique" (72.6/100 versus 74.8/100). En hétéro-évaluation, les enfants et adolescents transplantés avaient des scores de qualité de vie plus élevés que le groupe leucémie, sauf pour le "travail scolaire", les "relations amis" et les "loisirs". Les parents avaient des scores de QDV moins élevés par rapport aux Normes Françaises. Le sexe de l'enfant n'était pas un facteur prédictif contrairement au traitement immunosuppresseur, au niveau scolaire parental et à la fratrie.

**Conclusion**: La QDV pédiatrique ressort comme satisfaisante, celle des parents est inférieure à la population saine.
P5 : Kidney Re-Transplantation During Childhood: Feasibility and Outcomes

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Background: Over the last decade, kidney transplantation has increased amongst small children. Therefore we have observed a rise in re-transplantation during childhood, leading to surgical and medical challenges. This study looks into the characteristics of renal transplant recipients who have received or are waiting for more than one transplant during childhood.

Methods: This is a retrospective observational study in children in a single transplant centre between 2003 and 2016.

Results: During the study period, 191 paediatric kidney transplants were performed, of which 12 failed (6.3%) and 8 were re-transplanted (4.2%). Average ages were 4.8 and 9.3 years at first and second transplants respectively. Two patients underwent initial transplantation onto the aorta/IVC and then were re-transplanted onto the same vessels. Recurrent rejections caused graft failure in 8 patients (66.7%) and non-compliance was documented in 33%. None had disease recurrence as a cause for graft loss. 50% became HLA sensitized after the first transplant. 91.7% were CMV and EBV naive at the time of first transplant and 62% and 50% became CMV and EBV positive respectively before their second transplant. Three patients lost their second graft before they became adults, one of which received a third transplant at the age of 8 years. Graft survival of first compared to second transplant was 98% vs 88% at 3 year follow up.

Conclusion: The total re-transplantation rate is low in this cohort. Despite small recipient size, multiple kidney transplants during childhood are feasible but come with the extra burden of immunological, surgical and viral challenges. With this in mind, maximising first graft survival is imperative. 33% of patients had documented problems with medication compliance. We believe this to be a crucial area to focus upon in the fight for graft longevity in children.

P6 : Prophylaxis with valganciclovir of EBV infections in pediatric renal transplantation

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1 CHU Nantes, 2 CHU Rennes, 3 CHU Robert Debré, 4 CHU Lille, 5 CHU Necker Enfants Malades, 6 CHU Lyon Hôpital Femme Mère et Enfant, 7 CHU Montpellier, 8 CHU Toulouse, 9 CHRU Tours, 10 CHU Bordeaux, 11 CHU Strasbourg

Introduction: EBV primoinfection (PI) or reactivation is a serious concern in pediatric renal transplantation. Valganciclovir (VGC) is commonly used for CMV prophylaxis but its efficacy for EBV prevention is questionable.
**Patients and Methods:** Inclusion criteria were: recipients under 18y, renal transplantation performed between 01/01/2012 and 30/06/2013, EBV- recipient with an EBV+ donor (group at risk of PI) or EBV + recipients (group at risk of reactivation). VGC was administered for EBV or CMV prophylaxis, according to the common use in each center. A severe EBV infection was defined as a PTLD, a symptomatic infection and/or a high blood viral load (> 4.5 log/ml). Groups with prophylaxis (P+) or not (P-) were compared according to the data.

**Results:** 79 children were included, 72% in the P+ group, 28% in the P- group, 31% were in the group at risk of PI, 69% in the group at risk of reactivation. Incidence of severe EBV infection was 22.8% in the P+ group, and 22.7% in the P- group, (p=0.99). In the group at risk of PI, 42% of the patients of P+ had a severe EBV infection vs 33.3% in the P- group (p=1). There was no significant difference for severe EBV infection in the group at risk of reactivation (13% in P+ vs 18% in P-, p=0.68). Neutropenia was more frequent in the P+ group than in the P- group (66.7% vs 33.4%, p =0.005)

**Discussion and conclusion:** The results of this small cohort do not support the effectiveness of VGC for the prevention of EBV infection in pediatric renal transplantation. However, the risk of neutropenia is more frequent.

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**P7: Does rituximab and plasma exchange prevent disease recurrence in high risk FSGS following living donor transplantation?**

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Royal Manchester Children's Hospital

**Background:** For patients with end stage renal failure (ESRF) secondary to focal segmental glomerulosclerosis (FSGS), disease recurrence (DR) following renal transplantation (RT) is a significant concern. Patients with rapidly progressive primary disease, negative genetic screening and those with previous graft loss secondary to DR are most at risk. There is no consensus regarding the prevention and management of DR.

**Methods:** Four children with high risk FSGS, including 2 with previous graft loss due to DR, underwent living donor RT. All were managed with a uniform protocol of a single dose of rituximab (375mg/m²) 4 weeks prior to RT and 4 sessions of plasma exchange (PE) over the week prior to RT. DR was defined as urine protein:creatinine ratio >200mg/mmol on 2 consecutive days.

**Results:** One child with previous graft loss (Pt 1) had immediate DR and received PE for 5 months post-transplant. Another had immediate DR as well as impaired graft function and has had a partial response to PE. The third, who had previous graft loss (Pt 3) had DR at day 4 which responded to 5 sessions of PE. The fourth child has not had early DR.
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**Conclusions:** In this small cohort of patients with high risk FSGS, rituximab and PE pre-RT, did not reduce the risk of DR. However, in children with DR, including 2 patients with previous graft loss, the disease responds to PE. We are encouraged by our data to continue advocating the use of living donors for this difficult group of patients.
**P8: Impact of the genetic polymorphism of the cytochrome P450 on the metabolism of Tacrolimus in the pediatric kidney transplant**

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*CHU Strasbourg*

**Introduction:** Tacrolimus presents a narrow therapeutic index and its pharmacokinetic parameters are submitted to a high inter and intra-individual variability. An association between the polymorphism of the gene coding for the CYP3A5 and the hepatic metabolism level of the Tacrolimus was demonstrated. We distinguish a wild-type allele (CYP 3A5*1) and a mutant allele (CYP 3A5*3). The patients expressing the wild-type allele have a higher clearance of Tacrolimus. The aim of this study is to evaluate the influence of the genotype of the CYP3A5 in prescribed doses of Tacrolimus in a pediatric kidney transplant recipient population.

**Materials and methods:** a retrospective study, bicentrique, including 20 children kidney transplant recipients had been led. The genotyping of the CYP3A5 was realized by PCR method. The patients were divided into 2 groups according to the type of their allele (wild-type or mutated). Both group received Tacrolimus in the initial dose of 0.30 mg/kg/j. A blood residual monitoring of the rates of Tacrolimus (C0) was realized.

**Results:** on 20 children, 10 expressed the wild-type allele (group 1) and 8 expressed the mutant allele in the homozygous state (group 2). Whatever the genotype, we found a high inter and intra-individual variability. In the group 1, the doses of Tacrolimus were stable at 0.30 mg / kg / j, whereas in the group 2, we noticed a significant decrease of doses from day 30. Concerning the kidney biopsy at 3 months, there was no correlation between the genotype and the signs of nephrotoxicity.

**Conclusion:** it seems interesting to use lower doses of Tacrolimus for children expressing the CYP3A5 3/*3 because of a slower hepatic metabolism.

**P9 : Liver enzyme elevation following paediatric renal transplantation**

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**Background**

Paediatric data on the current prevalence and outcomes of liver dysfunction following renal transplantation is lacking. Liver enzyme elevation is a relatively common phenomenon within the adult population following renal transplantation and is reported to be higher following use of deceased donor kidneys.

**Methods**

Retrospective analysis of liver and renal biochemistry in renal transplant recipients between August 2010 and August 2015 was performed. Patients that were positive for
hepatitis B surface antigen (HBsAg), hepatitis C virus-antibody (HCV Ab) and those with preceding liver disease were excluded. Patients were grouped into those with abnormal liver enzymes within 3 months and 4 to 12 months following renal transplantation.

**Results**

Renal transplantation was carried out in 57 patients who fulfilled the inclusion criteria between 2010 and 2015. Elevated alanine aminotransferase (ALT) at more than 2 times the normal limit (>50 IU/L) was seen in 22.8% (13) of patients with an almost equal distribution between males (46%) and females (54%) at a median age of 10 years (range 3-14 years). Raised ALT occurred within 3 months of transplantation in all cases and did not vary significantly between deceased (20.6%) or living (25%) donor organ transplants. Liver enzymes normalised within 3 months in 12 (92.3%) with the majority normalising within 7 days (84.6%). Liver dysfunction was associated with use of IV antibiotics for urosepsis in 2 cases. No cause was found for the remainder. One patient has had a persistently elevated ALT following a living related donor transplant for 3 years with no cause found. None of our patients progressed to fulminant liver failure.

**Conclusions**

Elevated liver enzymes were found to be a common finding within our cohort of paediatric kidney transplant recipients. The majority of liver dysfunction is transient, occurring within 3 months of transplantation and resolving within 7 days.

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**P10: Temporo-spatial epidemiology of Idiopathic Nephrotic Syndrome in the Paris-area.**


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**Introduction** The etiology of Idiopathic Nephrotic Syndrome (INS) remains partially unknown. Environmental triggers such as viral infections have been reported associated with the onset of INS. The aim of this region-wide epidemiological study is to analyze the temporo-spatial patterns of INS.

**Methods** All children, aged 6 months to 15 years, living over the Paris area, with INS onset between December 2007 and May 2010, were included in a prospective multicentric study.

**Results** INS was diagnosed in 188 children, 93% of whom were steroid sensitive. Annual incidence was 3.35/100,000 children. A spatial cluster was further identified based on a kernel density mapping of cases and a nearest neighbor-hierarchical clustering approach. This area displayed a higher SIR 1.36 (95%CI 1.09-1.67). Temporal
analysis within this overincidence area showed seasonal variation, with a peak during winter period (p<0.01). In addition, the partition of Paris area in quintiles of population showed that the average delay of occurrence, with regard to the first study case, followed a longitudinal progression (p<0.0001).

**Discussion** The clustering of cases, the seasonal variation within this special area, and the progression over Paris area altogether suggest that INS may occur on an epidemic mode, involving environmental triggering factors. The geographic clustering of cases may further suggest the involvement of surface waters.

**P11: Treatment and follow-up in children steroid-resistant nephrotic syndrome: a retrospective single-center cohort of 68 patients treated by calcineurin inhibitors**

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**Introduction:** The treatment of idiopathic steroid resistant nephrotic syndrome (SRNS) is still challenging despite introduction of calcineurin inhibitors (CNI) based protocols, which dramatically improve the prognosis. The aim of this study was to report the long term follow-up and the impact of alternative treatments in a retrospective cohort of children with idiopathic SRNS treated with CNI.

**Methods:** We recorded data of all children with SRNS followed in our center between 1987 and 2013. Patients with secondary SRNS or genetic mutations were excluded.

**Results:** 68 patients (34 boys) fulfilled criteria. Mean age at diagnosis was 7 years and mean follow-up 7.1 years. All children had a biopsy and were treated with CNI (CsA 84%, FK 16%) in association with steroids for at least 6 months. Complete remission (CR) occurred for 41 of them (60%) and partial remission (PR) for 8 (12%). Multivariate analysis showed that young age at diagnosis and increase of albuminemia at the end of initial steroid therapy were associated with obtention of remission. For those who were CNI resistant, additional treatments such as plasma exchanges in 7 patients, immunoadsorptions in 8, and rituximab in 9 were proposed, with remission in respectively 1, 4 and 3 patients so that at the end, a CR was achieved in 47 patients (69%). Of these patients, 26 (55%) had at least one relapse. Evolution to end-stage renal disease (ESRD) occurred in 16 patients (23.5%) with post-transplant recurrence of NS in 88%, and graft loss in 31%. For patients without ESRD, immunosuppressive treatment was pursued during a median time of 5.2 years. Adverse events occurred in 77% of the patients.

**Conclusion:** Despite an improved prognosis since the introduction of CNI, idiopathic SRNS remains a severe disease, and there is a need for new treatments for multi-drug resistant patients and prevention of post-transplant recurrence.
Objectives: Tacrolimus is increasingly advocated as a steroid sparing agent in the management of nephrotic syndrome. As concerns exist about long term nephrotoxicity, interval renal biopsies have been advocated to detect early changes. Associations between histological changes and patient factors are not well established.

Methods: Single centre review of surveillance renal histology of children who received tacrolimus to treat nephrotic syndrome between 2002 - 2015. For consistency a single histologist independently re-analysed all histology.

Results: 26 children (16 male, 1 non-caucasian, 25 minimal change, 1 FSGS) commenced tacrolimus at median age 4.9 years (range 1.4 - 8.9). 7/26 (27%) of first biopsy taken after median duration 4.7 years (range 1.9 to 6.9) demonstrated features of calcineurin inhibitor (CNI) nephrotoxicity. Toxicity was associated with higher mean 12-hour trough serum tacrolimus levels: 0/11 showed toxicity with levels ≤ 4.36 to 5.54 µg/L vs. 7/15 (47%) with levels 5.69 to 7.36 µg/L (p <0.0001). No association was found with number of relapses, gender or duration of time on tacrolimus. Nephrotoxicity was mainly globally sclerosis or minimal chronic tubular changes.

10/19 patients without initial CNI toxicity underwent second biopsy at a median time of 5.0 (range, 1.8 – 6.7) years later. One developed toxicity. Estimated glomerular filtration rate in those who developed toxicity was normal. We attempted tacrolimus weaning in 20 patients: 11 patients relapsed, 4 within 2 months, further 5 within 1 year after dose reduction.

Conclusion: Significant number of children on tacrolimus showed histological nephrotoxicity after a short duration of therapy. In this small single centre experience, toxicity correlated with tacrolimus level rather than duration. A high number relapsed shortly following dose reduction. We suggest maintaining tacrolimus levels ≤5.5 µg/L to minimise nephrotoxicity.
Figure 1. Duration on tacrolimus and nephrotoxicity. * denotes patients with histological FSGS.

Fig 2. Average trough 12 hours tacrolimus levels from starting tacrolimus to first biopsy. Toxicity associated with higher levels: 0/10 showed toxicity with levels of 4.36 to 5.54 µg/L vs. 9/15 (60%) with levels 5.69 to 7.36 µg/L (p <0.0001).
P13: Epidemiology of childhood onset idiopathic nephrotic syndrome: a population-based study in Southern France

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Introduction: The estimated incidence of nephrotic syndrome (NS) ranges from 1.5 to 11.6/100,000 children per year but population-based studies are limited in Europe. The aim of this study was to determine the incidence and describe the initial characteristics of idiopathic NS in Southern France.

Methods: The study was conducted in 31 counties from 3 French regions (Nouvelle Aquitaine, Occitanie, Provence-Alpes-Côte d’Azur). An anonymized questionnaire was sent annually to all pediatricians from general hospitals, which were then returned to one referent physician in each University Hospital's Pediatric Nephrology unit from these regions. All children <15 years with newly diagnosed NS between 1 November 2014 and 1 October 2016 were included. Demographic, geographic, and limited clinical data were collected. To estimate incidence, denominators were obtained from the National Institute for Statistics and Economic Studies (INSEE). Five counties with missing data were excluded (13% of the population).

Results: One hundred and fourteen children with incident idiopathic NS were recorded in an area covering 14.5 million inhabitants. The calculated annual incidence during the study period was 2.2 per 100,000 children <15 years per year (confidence interval 1.8-2.6). The incidence was higher in urban vs. rural areas. Median age at diagnosis was 4.9 years (IQR 3.1-6.8) and median albumin was 14 g/L (IQR 10-17). In 32%, NS occurred following a viral infection and 8% presented complications in the acute phase including 2 patients with thromboembolic complications. 89% had steroid sensitive NS with a median time to remission of proteinuria of 9 days (IQR 7-14), 14% of whom requiring methylprednisolone pulses to achieve remission after a 4-week course of prednisone, and 11% had steroid resistant NS.

Conclusion: Although we had no alternative way to assess whether all cases of NS were identified, this population-based epidemiological study found higher or similar incidence to that of previous studies.

P14: Congenital Nephrotic Syndrome: How reliable is a raised alphafetoprotein in antenatal diagnosis?

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Background:
Congenital Nephrotic Syndrome (CNS) is an inherited autosomal recessive disorder. Mutation of NPHS1 gene is one of the most common causes of CNS. In a family known to
carry this mutation, raised maternal antenatal serum levels of alphafetoprotein (AFP) are highly predictive of an affected child.i, ii

Clinical details:
Review of white Caucasian family of whom one child has CNS.
Patient 1: Female born at 37+5, noted to have large placenta with a birth weight 3.1 kg. Postnatally, serum albumin 12g/L with urinary protein creatinine ratio (uPCR) of 2696mg/mmol. Clinical diagnosis of CNS made and subsequently confirmed on genetic analysis. Treated with albumin infusions, bilateral nephrectomies and a living related donor kidney transplant at 5yrs of life. Two post-transplant recurrences of nephrotic syndrome treated with steroids and albumin. Currently eGFR of 59.3mls/min/1.73^2 and urinalysis remains protein free.

Patient 2: Male, born at 39+1, normal placenta with a birth weight of 3.67 kg. 20 weeks antenatally, maternal raised AFP of 268.7kU/L (mean 60kU/L) leading to high suspicion of fetus being affected by CNS.iii Postnatally, initial uPCR 127mg/mmol with an albumin of 33g/L. Now 10 months old and thriving. Recent UPCR 159mg/mmol felt to be falsely elevated due to low urinary creatinine. Serum albumin stable at 35g/l and serum creatinine is 24µmol/L.

Genetic Results:
Patient 1: NPHS1 c.2335-1G>A intron 17 splice site pathogenic variant in homozygous state confirming a diagnosis of CNS.
Patient 2: Analysis of NPHS1 gene identified two heterozygous variants; a splice site variant c.2335-1G>A in intron 17 and a rare novel NPHS1 variant in exon 10, c.1295C>T, p.(Ser432Leu).
Parents: Heterozygotes on local genetic testing but await further detailed genetic testing.

Discussion:
The c.1295C>T variant is a very rare or possibly population specific variant that has not been reported in literature to date. Patient 2 demonstrates no manifestations of CNS despite high suspicion of diagnosis antenatally. We suspect this novel mutation is not pathogenic and patient 2 is a carrier of CNS.

Conclusion
The c.1295C>T, p.(Ser432LEU) is a newly identified genetic variant of uncertain clinical significance. AFP does not always accurately predict an antenatal diagnosis of CNS therefore antenatal counselling should be approached carefully.

Vitamin A Audit in Chronic Kidney Disease: Should we be measuring it routinely?

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Background: Dietary vitamin A is converted into retinol and is transported by the retinol binding protein after being stored in the liver. Impaired renal function leads to accumulation (Smith & Goodman, 1971) (Fassinger, Imam, & Klurfeld, 2010). High retinol levels are associated with increased intima-media thickness of the arteries, which is a marker of cardiovascular disease. It is also associated with abnormal osteoclast function and hypercalcaemia. There are no current guidelines in the UK regarding vitamin A intake and monitoring in CKD. A common practice is to limit intake to a maximum of twice the Reference Nutrient Intake value (Rees & Shaw, 2007). The KDOQI guidelines for Nutrition in Children with CKD suggest limiting the amount of oral intake of Vitamin A (Group, 2009).

Aims and Objective: This audit of practice looked at how frequently we test vitamin A levels in our department, how the levels compare with the normal reference values, and therefore whether there would be any merit in measuring Vitamin A routinely. We reviewed all patients with CKD Stages 4, 5, 5D and post renal transplantation from 2010 to 2016. Other nutritional biochemical markers measured were calcium, phosphate, triglycerides, cholesterol, vitamin D and vitamin E.

Results: Vitamin A measurements were done on 41 occasions in 25 patients out of a total of 189 in the last 6 years (6/25 on haemodialysis, 3/25 on peritoneal dialysis, 16/25 CKD 4&5 & post transplantation). Vitamin A was raised in 73% of dialysis and 73% of CKD patients. Only 28% of measurements were raised in transplanted patients. Despite only 26% of dialysis patients and 9% of CKD patients being hypercalcaemic at the time of sampling, Vitamin A showed a positive correlation with Calcium (p=0.01). It also showed an association with higher lipid and Vitamin E levels (p=0.0003).

Conclusion: Vitamin A should be measured routinely and dietary intake assessed. If addressed, it may lead to better control of calcium and lipid variables. We will add Vitamin A to our routine three monthly assessment blood tests, and adjust dietary intake accordingly.

Renal involvement in Glycogen storage disease type I: a cross sectional study

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**Introduction**: Glycogen storage disease type I (GSDI) is a rare autosomal recessive disease characterized by accumulation of glycogen and fat in liver and kidneys leading to development of chronic kidney disease whose mechanisms are currently poorly understood. Glomerular hyperfiltration is the first stage renal dysfunction but tubular abnormalities due to lipid and glycogen accumulation have also been recently described with the apparition of cysts development. The aim of this study was to characterize renal dysfunction in GSDI.

**Patients and Methods**: We studied retrospectively 21 patients with GSDI (median age 22 years [11-62]) followed in our centre between 1976 and 2016. Renal function was measured with inulin clearance and magnetic resonance imaging (MRI) was performed in all patients.

**Results**: Eighty five percent of patients had a dietary treatment, but only 45% had optimal metabolic control according to the ESGSD I criterias. Median GFR was 151 ml/min/1.73m² (range 97-209), 75% had glomerular hyperfiltration. No patient had chronic kidney disease but 30% had microalbuminuria. Thirty five % had metabolic acidosis; 36% had hypercalciuria, none of them had renal calculi. We found 31.2% of patients with nephromegaly, 15% with renal cysts. MRI can not detect overt glycogen/lipid deposition (no significant signal drop out in the MRI sequencing). No correlation was found between the GFR, albuminuria, signal drop in renal MRI and metabolic control.

**Discussion**: Hyperfiltration and tubular dysfunction was described in this cohort as previous reports. We detected nephromegaly and renal cysts in a minority of patients with no sign of renal glycogen accumulation in MRI.

**Conclusion**: Renal disease remains is a major complication of GSDI. GSDI patient could benefit of a regular tubular evaluation as well as kidney morphological assessment by echography and/or adequate MRI sequencing.

**P17: Pancreatic impairment and NPHP4 nephronophthisis.**

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**Introduction**: Nephronophthisis (NPHP), an autosomal recessive chronic tubulo-interstitial nephritis, is the most frequent genetic cause of end-stage kidney disease in childhood. Extra-renal manifestations such as retinitis pigmentosa, ocular motor apraxia, cerebellar ataxia, liver involvement or bone anomalies can be associated with NPHP in about 40% of cases. To our knowledge, isolated pancreatic abnormalities are not described in nephronophthisis.

**Case reports**: We herein report three children who carried nephronophthisis with NPHP4 mutations leading to end stage renal failure. They exhibit a particular isolated
pancreatic impairment. Two of them develop type 1 diabetes mellitus at early stage of life. Both exhibit pancreatic hypoplasia but exocrine function remained normal. The third case had also an asymptomatic pancreatic hypoplasia.

**Discussion**: To our knowledge, isolated pancreatic impairment had never been described in nephronophthisis. Our 3 patients exhibited a NPHP4 mutation. Recents works highlighted the rule of NPHP4 and NEK8 in the Hippo signaling pathway, a potent regulator of cell proliferation and organ size. That could be the key of pancreatic impairment in NPHP4 nephronophthisis.

**Conclusion**: This cases report lead to question about pancreatic impairment in patients suffering from nephronophthisis with NPHP4 mutations. For these patients, we suggest promoting pancreatic investigations in order to understand the physiopathology. Moreover, this cases report raised the question of simultaneous pancreas-renal transplantation when end stage renal failure occurred.

**P18: Anemia in infantile cystinosis: about one case**

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Cystinosis is a very rare autosomal recessive storage disorder caused by a defect in cysteine transport. Clinically, it is characterized by systemic accumulation of cystine crystals in tissues causing end-organ dysfunction in the kidney, eyes, muscles, and other organs in the body. Hematological symptoms are very rarely reported.

A 6-year-old boy was admitted with tiredness, pallor and fever for a few days. He had a very long medical history of cystinosis treated by cysteamine 4 times a day, since the age of one month. There was no evidence of splenomegaly and portal hypertension. He presented polyarthritis for a few months without inflammatory signs and biological abnormalities. He is treated with Methotrexate since 6 months, once a week without any improvement. At the same time, the cysteamine dose was decreased from 1.8 mg/m²/day to 1.1 mg/m²/day also without any improvement. Leukocyte cysteine level increased from 0.5 micromol/g of protein to 1.7 micromol/g of protein.

Blood cell count showed severe anemia (hemoglobin 5.3 g/dl) thrombocytopenia (platelets 54x10⁹/l ), leukocytosis (white blood cell 15.26 x 10⁹/l) with neutrophils (13.7 x 10⁹ G/L) and C-reactive protein 139 mg/l due to a pyelonephritis. An iliac bone marrow aspiration was performed and revealed a normal cellularity, normal megakaryocytic and erythroid precursors series, a moderate proportion of crystals stored in histiocyes. These crystals appeared refringent consistent with the diagnosis of cystinosis. The evolution was favorable after blood transfusion with out relapse after two months.

Cytopenia like anemia and thrombocytopenia without renal function impairment, were rarely reported in children with cystinosis. In our case it can be explained by infection.
Although rarely reported in literature, cystine crystals deposition in bone marrow in cystinosis seems to be common in this lysosomal storage disorder.

**P19: Losartan significantly lowers serum uric acid in hypertensive children with proteinuria**

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Serum uric acid (SUA) has emerged as a potentially modifiable risk factor for the progression of chronic kidney disease (CKD). We have previously reported the results of a trial showing that losartan and enalapril are comparable in their effects on proteinuria (KI 2013;28:737-743). In a post-hoc analysis of these patients, we determined the effect of losartan and enalapril on SUA over 36 months in 201 normotensive and 47 hypertensive children with CKD. Despite no overall difference between the two treatment groups the percentage change in SUA was significantly different between the two groups in hypertensive patients at 12 months; 3.69% decrease (95% CI (-3.93%, 11.31%)) with losartan vs. 12.57% increase (95% CI(3.72%,21.41%))with enalapril, p=0.007. This difference remained after 24 and 36 months of treatment (Figure). This effect was not observed in normotensive patients. Compared to enalapril, losartan significantly lowers SUA in hypertensive children with CKD. Studies are needed to evaluate whether changes in clinical practice, such as the preferential use of losartan over other antihypertensive agents, will slow progression in children with CKD.

![Graph showing the effect of losartan and enalapril on serum uric acid in hypertensive children over time.](image-url)
P20: Autosomal Dominant Polycystic Kidney Disease: Cardiovascular Manifestations in Children and Adolescents

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Introduction: This is a single-center study aiming to describe the cardiovascular manifestations of Autosomal Dominant Polycystic Kidney Disease (ADPKD) in children and adolescents and detect their relation with the age, kidney disease and type of gene mutation.

Material and Methods: We analysed data of 20 patients aged 5 to 19 (median 12) years old. Cardiovascular evaluation included 24 hour blood pressure (BP) monitoring, transcutaneous measurement of central aortic pressure, assessment of left ventricular mass index (LVMI), pulse wave velocity (PWV) and carotid intima-media thickness (IMT). Patients were classified based on percentile rank of reference values of these parameters in healthy children. 90th percentile was the cut-off point. Glomerular filtration rate (GFR) was estimated using the equation based on serum creatinine and cystatin C. Proteinuria was evaluated by a spot-urine microalbumin to creatinine ratio. Gene mutation was available in 15 patients.

Results: BP, IMT, LVMI and PWV were above the 90th percentile in 30%, in 45%, in 20% and in 23,5% of patients respectively. No relation was found between high BP and other vascular parameters. High LVMI and high BP were more frequent in children aged more than 14 (p=0,03) and more than 16 (p=0,011) years old respectively. High GFR (>120 ml/min/1,73m²) and microalbuminuria (microalbuminuria/creatinuria rate >2 g/mmol), which were found in 6 and 6 patients respectively, were not associated to cardiovascular manifestations. 3 type of gene mutation were detected: missense mutation in 6, nonsense mutation in 5 and deletion in 4 patients. After multiple square test, the type of gene mutation was significantly associated to high BP (p=0,044) and high PWV (p=0,006); deletion was the incriminate gene mutation.

Conclusions: Cardiovascular manifestations of ADPKD are present even in normotensive children and adolescents and don't seem to be related to the chronic kidney disease. Deletion of PKRAD gene is associated to the early cardiovascular manifestations.

P21: Renal replacement therapy in children with methylmalonic academia

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**Introduction:** Methylmalonic acidemias are rare congenital metabolic diseases of the catabolic pathway for branched amino acids, long-chain fatty acids and cholesterol, that lead to the accumulation of methylmalonic acid (MMA) in the blood, urine and cerebrospinal fluid. The evolution is marked by acute decompensations and chronic complications including neurological, renal and cardiac damage. Renal dialysis is a key element of the treatment of these patients but little data exist in the literature on its outcome.

**Methods:** We retrospectively reviewed the charts of 5 children who were treated at Necker Hospital for methylmalonic acidemia and required dialysis based on renal or metabolic indications. We compared the methylmalonic acid plasma levels depending on the dialysis method and the intervals between the blood sampling and the dialysis sessions.

**Results:** We observed a trend to lower MMA plasma levels among children in hemodialysis compared to those in peritoneal dialysis but without any statistically significant difference (p=0.09). The median plasma MMA reduction coefficients were higher in the hemodialysis group (82-89%) than in the peritoneal dialysis group (14-35%). In both groups, we noticed a rapid increase of plasma MMA levels between 2 dialysis sessions.

**Discussion:** Despite the above-mentioned variability in the plasma MMA levels between dialysis sessions and between the 2 treatment methods, the quality-of-life of the 5 patients were dramatically improved with a decrease in the number of hospitalizations for metabolic decompensations and a safe increase in protein intake.

**Conclusion:** These observations illustrate the efficiency of renal dialysis in methylmalonic acidemia. However, optimized dialysis strategies are needed to avoid the rapid increase in MMA levels observed in the interdialytic period and potential MMA complications. Continuous peritoneal dialysis could be a good option. We are currently using this technique for one patient and the preliminary results are encouraging with a significant stable reduction of plasma MMA, improvement of his general condition and correction of hematological anomalies.

**P22: Nephronophthisis in children : phenotypes and genotypes. A single centre experience**

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**Introduction:** Nephronophthisis (NPHP) account for 5 to 10% of end stage renal failure (ESRF) occurring in children. Different extra-renal phenotypes have been described and mutations in 20 different genes have been reported all of it coding for proteins that localize to the primary cilium. We report here on the renal and extra-renal phenotypes and on the genotypes of 22 children diagnosed with NPHP in Montpellier between 1989 and 2015.
Methods: The medical records of the patients were analyzed for their renal phenotypes, extra-renal symptoms, genetics results and follow-up.

Results: 22 children of 20 families were diagnosed as having NPHP. The sex ratio was 1.2 M/F. Median age at diagnosis was 6.3 years (0.4 to 14). Only 7 patients have an isolated renal phenotype, the remaining 15 having extra-renal symptoms: Senior Loken syndrome (SLS) (n = 7), Joubert syndrome (JS) (n=5), hypoplastic pancreas with insulin dependant diabetes mellitus (n=1), hepatic fibrosis and cones epiphysis (n=1). Genetics testing were available for 19 children. The mutations were: NPHP1 (n=7), NPHP1 and NPHP5 (n=1), NPHP2 (n=1), NPHP4 (n=1), NPHP5 (n=3), NPHP6 (n=1), NPHP12 (n=2), NPHP20 (n=3). 16 patients reached ESRF (6 at diagnosis) at a mean age of 9.4 years. 15 have been transplanted.

Discussions: NPHP is an important cause of genetically transmitted CKD in children, with often a late diagnosis, especially in the absence of extra-renal symptoms. Worthy of note only 7/22 patients have no extrarenal features. SLS and JS are the more frequent diagnosis in case of syndromics NPHP. Mutations were found in 7 over the 20 genes already described in NPHP. The fastest evolution to ESRF was seen in the patient with the juvenile form (NPHP2) and in the patient harboring mutations in both NPHP5 and NPHP1. JS and SLS were associated in our patients with differents mutated genes: NPHP1, NPHP5, NPHP6, NPHP20. To date, 15/16 children with ESRF have been transplanted, 3 of them having severe mental retardation.

P1: Predictive markers of functioning of peritoneal dialysis catheters in pediatrics: the angle on the abdominal X-ray, is it predictive?

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Introduction: In peritoneal dialysis (PD), mechanical complications affect 1 catheter out of 5, with loss of the catheter in 37% of cases. A study [Bammens,2014], described that mechanical complications could be predicted according to the catheter tilt angle on the abdominal X-ray, in adult. We have studied in pediatric the catheter tilt angle on the abdominal X-ray tried to determine its role in catheter operation.

Patients and methods: A bicentric retrospective study has been realized from 2010 to 2015, including 37 children in PD. We have reread all the postoperative images, after the initial placement of the catheter, and those made when mechanical complications occurred (n=59). The angle of the “swan neck” portion of the catheter and an imaginary horizontal line has been measured. Four sections of angles have been identified: <50°, 50-90° and ≥ 90°, unmeasurable when ≥ 180°.

Results: 27.1% of children were reoperated on, related to catheter mechanical complications. Among these catheters with mechanical complications, 66.6% had an angle <50°, 30% had an angle between 50° and 90°, and 55.2% an angle ≥ 90°. 44.1% of
the catheters didn’t show any malfunctions, among them: 70% had an angle between 50 and 90°, 44.7% an angle ≥ 90° and 33.3% an angle <50°.

**Discussion:** The catheters showing the most complications were those with an initial angle of placement ≥ 90° and with an angle <50°, on the abdominal X-ray. Angles between 50° and 90° were the least complications providers. A larger study will confirm these data, in order to correct the position of the catheter analyzed by radiology, in intra operative.

**P2**: Emergency peritoneal dialysis in children: EPH DASKI Dr. Constantine experience

S. MISSOUM

**EPH DAKSI CONSTANTINE, ALGERIA**

**Introduction:** Peritoneal dialysis (PD) in emergency is very often required in pediatric resuscitation as the only possible to extra purification kidney including technique because of the small weight of these patients.

**Patients and methods:** over a period of a year (may 2015 - August 2016) we have identified 12 children who required the DP in emergency, including 8 boys and 4 girls, the average age is 10 months (extremes of 2 months to 36 months), the average weight of 6 kg (4to13kg). The volume of the solution of dialysis in each exchange varied between 10 and 20 cc/kg during the first 48 hours then gradually increased up to 30-40 cc/kg, the time of stasis between 30 and 60 min, used solutes are the isotonic. All these parameters vary from one patient to another according to the goal.

**Results:** On our 12 small children, 08 suffered from acute kidney injury (AKI) (4 septic shock, 3 drug toxicity, 01 hemolytic uremic syndrome) and a fortuitous discovery of end stage renal disease (ESRD) in 4 requiring dialysis in emergency (4 urinary malformations). One death was due to complications of the initial pathology (septic shock). The average number of peritoneal exchanges to normalize the hyperkalaemia was 4 (2-6), to normalize the rate of urea, it took on average 8 exchanges (6-10), to totally eliminate the sodium and water overload (euvoolemia) 15exchanges. We had leaks or peritoneal infection, the most frequent complication was paradoxically hypokalemia. In the cases of AKI, the recovery of renal function was total in 100% of cases. For the cases of ESRD, passage in APD (after a short period in CAPD) and record pre kidney transplant if the weight allowed.

**Discussion:** Our results are quite encouraging, we learned adapting the techniques of the RFP has each case, recruitment is facilitated because of the existence of 3 paediatric services to Constantine, the RFP in emergency in children has small weight is increasingly present in our daily lives (60% of our children in DP).

**Conclusion:** the RFP in emergency in children is not only a necessity imposed by the weight barrier but a method has full and extremely effective.
P3': Systematic prescription of automated technique peritoneal dialysis in children: medical need or social gesture?

Dr S. MISSOUM

EHS DAKSI CONSTANTINE

Introduction: Automated peritoneal dialysis (APD) is a technique of peritoneal dialysis (PD) to allow not only short and repeated cycles without too much manipulation but also an increased social life. APD is especially indicated for the hyper-permeable peritoneal membranes and at anuria, but should children on PD be systematically put on APD?

Patients and methods: Over a period of 5 years (2012-2016) we identified 12 children in ESRD benefiting from the APD as an extra kidney treatment. We included all children 0-16 yrs, and carried out a PET test periodically (every 6 months), assessed the residual diuresis and identified the number of peritoneal infections.

Results: 12 children, 8 boys and 4 girls with an average age of 12 years (18 months - 16 years) at the beginning of the APD, the average length of the technique is of 4 years (3-5 years). The foremost nephropathy is malformative uropathy for the younger ones. PETs made at 6 months and one year identify hyper-permeable peritoneum in 100% of the cases, those done at 3 years reveal that for 50% of the children, the peritoneum is moderate to hypo-permeable. PETs at 5 years reveal that 70% of the peritoneum have become hypo-permeable. Diuresis is still kept at all children probably due to initial kidney disease (chronic interstitial nephritis). The average number of episodes of peritoneal infections is 2/year. The peritoneum became increasingly hypo-permeable with the time on PD (beyond 3 years) and the number of the peritoneal infections (beyond 8 episodes) but also with age. In fact the older the child is, the less hyper-permeable his peritoneum is.

Conclusion: APD in children early in his life in renal extra treatment seems a medical necessity that fades seriously over time. The need of peritoneal assessment continues in PD.

P4': Acute pancreatitis in pediatric patients undergoing hemodialysis, our experience.

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Introduction: Several case reports and studies suggest that the risk of acute pancreatitis is increased in patients with end-stage renal disease undergoing peritoneal dialysis (PD) as compared to those undergoing haemodialysis (HD) treatment. It has not been described in pediatric patients. We report 2 cases of teenagers who developed severe acute pancreatitis while undergoing hemodialysis.
**Case 1**: A 17 year-old patient, has been undergoing hemodialysis for 1 year due to a recessive Alport syndrome. She developed acute necrotizing pancreatitis (Balthazar score D). Imaging studies revealed pancreatic enlargement with inflammatory exudates. Local complications such as « walled-off necrosis » and pseudocyst developed, causing pain and threatening adjacent organs. After failure of conservative treatment (prolonged IV sandostatin and continuous enteral nutrition), an endoscopic transmural drainage was performed at month 3. Clinical improvement was dramatic.

**Case 2**: A 17 year-old patient, undergoing hemodialysis for 4 months due to sequelae of post Shigella hemolytic uremic syndrome, presented with an acute necrotizing pancreatitis (Balthazar score E). Evolution was rapidly favorable under conservative treatment (IV sandostatin and continuous enteral nutrition).

No obstructive, genetic, infectious or toxic etiology, was found in both patients. They had no history of recent hyperparathyroidism, hypercalcemia or hypertriglyceridemia.

**Discussion and conclusion:** Acute pancreatitis in end stage renal disease are more frequent than in general population. It is considered as a multifactorial disease, with the risk of the general population, the risk related to uremia, hypercalcemia, hypertriglyceridemia and alcohol abuse. In our patients, alteration of pancreatic microcirculation due to repeated ischemic events during the hemodialysis sessions (bradykinin and subsequent nitric oxide release) may have triggered the process leading to acute pancreatitis. Acute necrotizing pancreatitis can occur in pediatric age patients, and early diagnosis should be performed whenever acute epigastralgia with or without hemodynamic changes occur.

**P5**: Arterio-venous fistula hemostasis in a pediatric hemodialysis centre

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**Introduction:** Arterio-venous fistula (AVF) is the most common, effective and lasting vascular access for hemodialysis (HD). However, it may cause some complications such as post-dialysis bleeding from puncture site.

**Materials and Methods:** Ten patients were enrolled. Information regarding clinical and biological data, hemostatic measures, patients and nurses practices and feelings, were collected from the beginning of HD session to disconnection step. We sought to assess post-dialysis AVF bleeding risks.

**Results:** Four girls and six boys with an average age of 11 years were included. Primary diseases were mainly CAKUT and nephrotic syndrome. 3 patients were on a long-term anticoagulation for thrombophilia and femoral thrombi, their average INR was 2,2. Hypertension was frequent. Average hemoglobin was 11.7 g/dl with anemia <11.5 g / dL in 3 patients. Thrombocytopenia <200x10^9/ L was noticed in 4 patients. Mean fractional excretion of urea was 81%. AVF complications were observed in 5 patients with aneurysm, stenosis and high-flow AVF requiring surgical management. At HD disconnection, first-line hemostatic gauzes were used for a patient with post-dialysis bleeding antecedent in Coumadin overdose circumstances. Average compression time was 10,4'. Regarding patients feelings about this post-dialysis step, most of them showed no anxiety, feeling painless and stressless. However, one patient with a history
of hemostatic complications felt stressed and anxious. Concerning nurses, they felt stressed in only this case with prolonged bleeding antecedent.

**Discussion:** To our knowledge, no studies have analyzed AVF hemostasis in children on HD. Bleeding diathesis in chronic uremic patients is mainly due to abnormalities in primary hemostasis, anemia and certain dialysis medications. HD therapy itself leads to various hemostatic changes. AVF mechanical complications can also cause bleeding issues. Screening for AVF complications is very important through regular clinical and imaging checking in order to manage them on time. It’s also major to prevent anticoagulation overdose risks, to optimize urea dialysis and to improve anemia management.

**Conclusion:** Results from our pediatric study showed that post-dialysis bleeding risk factors are mainly high-flow AVF, hypertension, anticoagulation, uremia and anemia. Prevention and early treatment of AVF complications are essential to avoid bleeding issues.

**P6**: Efficacy of Immunoadsorption in Anti-Glomerular Basement Membrane Glomerulonephritis in Children: Case Report and Literature Review

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**Introduction** - Anti-glomerular basement membrane glomerulonephritis (anti-GBM GN) is a rare autoimmune disease characterized by rapidly progressive glomerulonephritis that may be associated with pulmonary hemorrhage. Anti-GBM GN is caused by auto-antibodies directed against the α3 subunit of type IV collagen. Without any appropriate treatment, the disease is generally fulminant, and patient and kidney survival is poor. The current guidelines recommend the use of plasma exchanges and immunosuppressive drugs. Immunoadsorption that removes pathogenic IgGs from the circulation and does not require plasma infusions has been seldom used in adult patients with good tolerance and efficiency.

**Case report** - We report the first pediatric case successfully treated with immunoadsorption combined to immunosuppressive drugs in a seven year-old girl who presented acute kidney injury (eGFR 38mL/min/1.73m²) with >80% glomerular crescents and linear IgG deposits along the GBM. Ten immunoadsorption sessions led to rapid and sustained clearance of auto-antibodies, and improvement of kidney function until 21 months after onset (eGFR 87mL/min/1.73m²). No adverse effect was noted.

**Discussion and literature review** - 27 pediatric cases were reported with a mean age at diagnosis of 8.76±4.6 years, and a sex ratio of 1:3 (M/F). Patient and renal survival were similar to adult populations. Five children died within the first 2 months. 12/27 (44 %) had an independent renal function after a mean of follow-up of 2 years (1d-10yrs). Among the 14 dialyzed patients, only 3 recovered an independent renal function. 13/20 (65%) had >80% crescents and all died or reached ESKD contrary to the 7
patients with <80% crescents who were alive with independent renal function at last follow-up. 15% of children underwent renal transplantation compared to 12% in recent adult study. Pulmonary expression was less represented in children (54% vs. 70-80%).

**Conclusion** - This report adds to the growing body of evidence suggesting immunoadsorption as a therapeutic alternative to plasma exchanges in pediatric anti-GBM GN.

**P7'** : Vascularite à ANCA compliquant un Syndrome Néphrotique Idiopathique (SNI) révélée par une conjonctivite prolongée.

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**Introduction** : Nous rapportons un cas clinique de vascularite à ANCA compliquant l’évolution d’un syndrome néphrotique idiopathique. L’association entre SNI et vascularite à ANCA est exceptionnelle. La persistance d’une conjonctivite a permis d’évoquer ce diagnostic avant l’insuffisance rénale terminale.

**Observation** : Une adolescente de 17 ans suivie pour un SNI depuis l’âge de 5 ans a présenté une arthrite de cheville droite associée à une conjonctivite de l’œil gauche. Son bilan initial montrait : Hb:12,5g/dL ; GB:5000/mm3 ; Plaquettes:531000/mm3; CRP:60mg/L ; Créatinine:66µmol/L ; Albumine:43g/L ; Protidémie:81g/L ; Rapport PU/CU:12mg/mmol.

Après 4 semaines, le contrôle de la fonction rénale a révélé une insuffisance rénale aigue avec : créatinine:296µmol/L ; Urée:9,1mmol/L ; Protides:75g/L ; Rapport PU/CU:61,8mg/mmol. Les ANCA à 640UI/mL de spécificité anti-PR3 à 90 UI/mL, qui avait été demandés à titre systématique, ont permis de débuter en urgence les bolus de méthylprednisolone 72h avant réalisation d’une ponction biopsie rénale confirmant la glomérulonéphrite nécrosante pauci-immune.

**Prise en charge thérapeutique et évolution** : Malgré 3 bolus de méthylprednisolone et un premier rituximab précoce, la récupération de la fonction rénale n’a été obtenue qu’après 9 échanges plasmatiques. Le maximum de créatinine a été de 647 µmol/l à 26 jours du premier bolus. La fonction rénale à 8 mois de recul montre une créatinine à 105 µmol/l et un rapport PU/CU à 20 mg/mmol. Le traitement d’entretien comprend des injections de rituximab tous les 6 mois pendant deux ans avec un objectif de corticothérapie à 10mg/jour à 6 mois et 5mg/jour à un an.

**Conclusion** : L’apparition de signes extra-rénaux : arthralgies ou conjonctivite trainante doit faire évoquer une vascularite. Les vascularites à ANCA sont une urgence diagnostique et thérapeutique. Cette observation soulève la question du dosage des ANCA au diagnostic et lors du suivi des syndromes néphrotiques dit « idiopathiques ». 


ANCA vasculitis complicated an idiopathic nephritic syndrome revealed by a prolonged conjunctivitis

Introduction: We have reported a case of ANCA-associated vasculitis complicating the course of an idiopathic nephrotic syndrome. The association between INS and ANCA-associated vasculitis is exceptional. The persistence of a conjunctivitis made us consider this diagnosis before end stage renal failure.

Case Report: A 17 years old teenager monitored for INS since the age of five presented a right ankle arthritis associated with a left eye conjunctivitis. Her initial blood test showed: Hb: 12.5 g/dL, WBC: 5000/mm3 Platelets: 531000/mm3; CRP: 60 mg/L; Creatinine: 66μmol/L; Albumin: 43g/L; Protein: 81g/L; urine protein to creatinine ratio: 12 mg/mmol. The monitoring of renal function 4 weeks later showed an acute renal failure with creatininemia up to 296μmol/L; Urea: 9,1mmol/L; Protein: 75g/L; urine protein to creatinine ratio: 61,8mg/mmol. The antibody systematic screening showed positive ANCA (640UI/mL) with anti-PR3 specificity up to 90 IU/L. This allowed us to start methylprednisolone pulses 3 days before performing a kidney biopsy which confirmed the pauci-immune necrotizing glomerulonephritis.

Therapeutic management and development: Despite 3 methylprednisolone pulses and an early first rituximab, the renal function recovery was only achieved after 9 plasma exchanges. The maximum creatinine level was 647 μmol/L 26 days after first methylprednisolone pulse. Creatinine level 8 months later is 105 μmol/L with an urine protein to creatinine ratio at 20 mg/mmol. Maintenance treatment includes rituximab injection every 6 months for two years and corticosteroid therapy with an objective of 10mg/day at 6 months and 5mg/day to a year.

Conclusion: The appearance of extra-renal signs such as arthralgia or conjunctivitis should suggest vasculitis. ANCA vasculitis is a diagnostic and therapeutic emergency. This case report raises the question of ANCA dosing at diagnosis and during monitoring of nephrotic syndrome considered as « idiopathic ».

P8': A useful biomarker for diagnosis of a polyuria polydipsia syndrome in a 7 month old child

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Introduction: Diabetes insipidus is characterized by hypoosmotic polyuria related to deficiency of Arginin Vasopressin (AVP) secretion (Central Diabetes Insipidus (CDI)) or
renal insensitivity to AVP (Nephrogenic Diabetes Insipidus (NDI)). The water deprivation test with assessment of AVP activity is currently the gold standard for differential diagnosis in patients presenting primary polydipsia, CDI and NDI. Nevertheless, it can be dangerous without proper surveillance and its interpretation may be challenging, especially for partial diabetes insipidus. Other markers have been suggested. AVP measurement is not sufficient for precise diagnosis, as it is an unstable pulsatile hormone with a very short half-life. It comes from the prohormone preprovasopressin with concomitant release of copeptin (C-terminal moiety of preprovasopressin) in an equimolar ratio. Plasmatic copeptin, a stable 39 amino acid glycopeptide, is much more stable in vitro and its measurement is easier and faster (<4h). Past studies have shown greater sensitivity and specificity of copeptin versus AVP to discriminate etiologies of polyuria-polydipsia syndrome in adults, but its value has not been demonstrated in infants yet.

Observation: We report the case of a 7 month-old infant who presented poor weight gain and polyuria-polydipsia syndrome. The laboratory tests pointed out severe hypernatremia (170 mmol/L), blood hyperosmolarity (330 mOsm/L) with inappropriate urinary hypoosmolarity (168 mOsm/L). Plasmatic copeptin measurement was found in a very high level, 303 pmol/L (1-14 pmol/L). DdAVP administration did not improve the polyuria, confirming the final diagnosis of NDI. Hyperhydration with hypoosmolar diet normalized within a week hydration status and circulating levels of copeptin.

Conclusion: Copeptin, a stable peptide reflecting vasopressin's secretion, could be a safer and faster biomarker for etiological diagnosis of polyuria-polydipsia syndrome in children. Further investigation is needed in order to establish pediatric normal range.

P9': A multidisciplinary minefield

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We present the case of a young boy, now 2 years of age, with a rare variant of the bone marrow failure syndrome, Fanconi anaemia, not expected to survive infancy. He has an ectopic pelvic kidney with associated chronic kidney disease and is approaching the need for renal replacement therapy. He currently also requires fortnightly platelet transfusion. Fanconi anaemia is typified by multiple congenital anomalies, progressive aplastic anaemia and a predisposition to malignancy.

Boy J was born at 34 weeks gestation, after a pregnancy complicated by oligohydramnios and severe symmetrical intrauterine growth restriction. His congenital abnormalities include ventriculomegaly, imperforate anus, bilateral absent radii, ectopic pelvic kidney and hypoplastic lungs. His diagnosis was confirmed through chromosome fragility testing after his array of anomalies and falling platelet count suggested a possible Fanconi diagnosis. Subsequent next generation sequencing went on to identify a hemizygosity in exon 8 of the FANCB gene on chromosome X. His particular phenotype
(VACTERL-H (hydrocephalus)) has been described in only 4 other cases of FANCB mutations in the medical literature. Interestingly the facial phenotype is strikingly similar between cases. His survival and quality of life are a testament to the patient centred approach to his care and the exceptional multidisciplinary working that has been required throughout. His case also highlights the importance of strong links between tertiary nephrology and secondary paediatric care.

We describe the challenges encountered, discuss the important ethical issues that have been raised along his journey, in particular relating to the potential need for bone marrow transplant and renal replacement therapy (of which there is no international experience in FANCB cases), and illustrate the specifics of his phenotype with the aid of some fascinating pictures. His case provides valuable additional insight into this rare variant of Fanconi Anaemia.

P10': Ureteropelvic junction obstruction in the solitary kidney in children: future of the renal function after pyeloplasty


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Aim of the study. Ureteropelvic junction obstruction (UJPO) in solitary functional kidney may result in chronic kidney disease (CKD), but long-term data are scarce. We evaluate renal function after pyeloplasty for the treatment of UJPO on children in the setting of a solitary kidney.

Methods. 31 patients with solitary kidney underwent classic Henderson-Hynes pyeloplasty: posterior lombotomy (n=25), retroperitoneoscopy (n=5) and one laparotomy. Solitary functional kidney was due either to contralateral non-functional kidney (n=28) or to renal agenesis (n=3). Four patients had an associated uropathy (bladder extrophy, urethral duplication, posterior urethral valves, obstructive megaureter). Indication for pyeloplasty was prenatal diagnosis of hydronephrosis with increasing renal pelvis dilatation on follow-up (n=15), renal failure in the neonatal period (n=10), urinary tract infections (n=4) and flank pain (n=2). Serum creatinine, blood pressure, height and weight were measured preoperatively, and at all post-operative follow-up examinations.

Main results. Median age at surgery was 5.3 months (10 days-15 years). Median follow-up after surgery was 7.3 years (0.6-33.8 years). At last follow-up 10 (32%) children had CKD: 5 had CKD stage 2, 4 had CKD stage 4 and the last patient was successfully
transplanted at 2 years of age. Among the 10 children operated because of a neonatal renal failure, 7 (70%) had CKD.

**Conclusion:** UJPO in solitary kidney in children is associated with a high prevalence of CKD, especially in patients with neonatal renal failure and warrants long term renal function follow-up.

**P11': Prognostic value of microbiological investigations in Escherichia coli related Hemolytic Uremic Syndrome in children.**

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**Introduction:** Post-diarrheal hemolytic-uremic syndrome (HUS) secondary to Shiga toxin-producing _Escherichia coli_ is a clinical triad of microangiopathic hemolytic anemia, impaired renal function and thrombocytopenia, and is the main cause of acute kidney failure in children under 3 years, and its severity is still difficult to predict. The aim of this study was to assess whether the strain typing and virulence factors characterization could help clinicians to predict the level of renal impairment and the complications of HUS, amongst the already described prognostic factors.

**Methods:** Clinical and laboratory data of all pediatric patients referred to one of the three pediatric nephrology department of Ile-de-France between 2009 and 2014 for a post-diarrheal HUS with microbiological analysis available, have been included.

**Results:** 77 patients were included, 97% of them were infected with _E. coli_ secreting Stx2. Within the subgroups, Stx2d appears to be protective against dialysis (OR 0.006, 95% CI [0.57 0.001]). When associating Stx2d with already known severity criteria, it increases the predictive power of dialysis risk (c-statistic 0.96 against 0.88 without adding Stx2). No predictive microbiological factor for dialysis duration or neurological complication was found. Of note, non specific complement factor activation was significantly associated with the risk of dialysis, prolonged duration of dialysis, and neurological complications.

**Conclusion:** Toxin and strain characterization in HUS still have a major epidemiological interest but does not help predicting clinical complications.

**Discussion:** Genome sequencing could bring new implications in clinical characterization of the disease.

**P12': Performances diagnostiques de la bandelette urinaire pour le diagnostic d’infection urinaire chez les enfants de moins de 3 mois.**
Introduction : Certaines études récentes suggèrent qu'une bandelette urinaire (BU) négative pour les leucocytes et nitrites est suffisante pour s'affranchir d'une mise en culture systématique des urines chez les enfants de moins de trois mois.

Méthodes : Cette étude rétrospective a inclus l'ensemble des enfants de moins de 90 jours avec une BU et un examen cytobactériologique des urines (ECBU) réalisés aux urgences pédiatriques du CHU de Nantes entre le 1er janvier 2014 et le 30 juin 2015. Les performances diagnostiques ont été calculées en comparant le résultat de la BU au résultat de la culture urinaire et au diagnostic final de pyélonéphrite aigue (PNA) établi de façon rétrospective pour chaque dossier. Le seuil de bactériurie positif est différent selon les recommandations, plusieurs seuils ont donc été étudiés (10^3, 10^4 ou 10^5 CFU/ml) pour considérer la culture comme positive.

Résultats : 615 enfants ont été inclus. La BU a présenté une sensibilité entre 56,6 et 91,2%, une spécificité de 97,2%, en fonction du seuil de bactériurie analysé (10^3, 10^4 ou 10^5 CFU/ml), avec un rapport de vraisemblance positif (RVP) entre 19,8 et 32 et un rapport de vraisemblance négatif (RVN) entre 0,09 et 0,45. La probabilité pré-test de PNA dans notre étude est de 24.9% chez le garçon et 5.4% chez la fille. La probabilité post-test de PNA en présence d'une BU négative est comprise entre 2,1% à 12,6% chez le garçon et de 1,2 à 2,8% chez la fille, selon le seuil de bactériurie considéré.

Conclusion : Nos résultats sont en faveur d'une mise en culture systématique des urines chez le garçon de moins de trois mois, mais pas chez la fille d'un à trois mois en cas de négativité de la bandelette urinaire. Chez l'enfant de moins d'un mois, la réalisation d'une culture urinaire doit rester systématique.

Urinary dipstick performances for the diagnosis of urinary infection in children less than 3 months

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Introduction : Recent studies suggest that a negative urinary dipstick (UD) for leucocytes and nitrites is reliable and do not have to be confirmed by urinary culture, even in children less than 3 months.

Methods : This retrospective study included children aged less than 90 days in whom an UD and an urinary culture had been performed in the emergency department of the university hospital of Nantes, from the 01/01/2014 to 30/06/2015. UD performances were calculated comparing the results of UD to the results of urinary culture and to the final diagnosis of acute pyelonephritis (APN) which was retrospectively considered for each case. Significant bacteriuria thresholds are different according to guidelines, so several bacteriuria levels were considered as significant for 10^3, 10^4 and 10^5 CFU/ml.

Résultats : 615 children were included. The sensibility of UD varied from 56,6 to 91,2% according to the bacteriuria threshold of 10^3, 10^4 or 10^5 CFU/ml respectively, the
specificity is 97.2%. The likelihood positive ratio varied from 19.8 to 32 and the likelihood negative ratio from 0.09 to 0.45 according to the bacteriuria levels. The pre-test probability of APN was 24.9% in boys and 5.4% in girls in our cohort. The post-test probability of APN in the case of a negative UD was 2.1% to 12.6% in boys and 1.2 to 2.8% in girls, according to the bacteriuria levels.

**Conclusion**: These results suggest that a negative UD is not reliable enough and urinary culture seemed to be necessary for boys aged less than 3 months, but not for girls aged from 1 to 3 months.

**P13': Insuffisance rénale aigue sévère et anti-inflammatoire non stéroïdien**


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**Introduction**: Les anti-inflammatoires non stéroïdiens (AINS), fréquemment utilisés, sont prescrits à visée antipyrétique dans 25% des cas. Leur néphrotoxicité est responsable d’environ 1 à 5% des insuffisances rénales aigues (IRA) de l’enfant. L’hypovolémie ou l’atteinte rénale préexistante majorent la néphrotoxicité des AINS. Les AINS sont responsables d’une hypo perfusion rénale par diminution de synthèse des prostaglandines entraînant alors une nécrose tubulaire aigue (NTA). Les AINS peuvent être aussi à l’origine d’une réaction immuno-allergique entraînant une néphrite tubulo-interstitielle aigue (NTIA).

**Observations**: Nous rapportons 3 cas d’IRA sévères suite à la prise d’ibuprofène à dose thérapeutique, pendant une courte durée. Aucun enfant n’avait d’antécédent néphrologique.

*Cas n°1*: Prise d’ibuprofène chez une fille de 4 ans dans un contexte de virose ORL et vomissements. L’enfant était anurique avec une créatinine maximale de 850µmol/l. Une épuration extra-rénale était débutée rapidement. L’histologie mettait en évidence une NTIA sévère associée à une NTA. L’évolution était défavorable avec une insuffisance rénale chronique terminale nécessitant une dialyse.

*Cas n°2*: Prise d’ibuprofène chez un garçon de 8 ans dans un contexte de pleuropneumonie et vomissements. La créatinine maximale était à 320µmol/l. La diurèse était conservée. L’évolution était rapidement favorable après réhydratation et arrêt des AINS. Le diagnostic retenu était une NTIA post AINS (la ponction biopsie rénale n’a pas été réalisée).

*Cas n°3*: Prise d’ibuprofène chez un garçon de 5 ans dans un contexte de pneumonie et vomissements. L’enfant était oligo-anurique avec une créatinine maximale à 490µmol/l. L’histologie retrouvait une NTA et des lésions de glomérulonéphrite aigue. L’évolution était favorable.
Conclusion: Les AINS sont toxiques et entraînent des IRA sévères, notamment en cas d’hypovolémie. Les manifestations cliniques et biologiques peuvent être variées, seule l’histologie rénale confirme le type d’atteinte rénale. La ponction biopsie rénale est donc intéressante dans la prise en charge. Ces pathologies sont évitables, le paracétamol reste l’antipyrétique de choix.

Severe acute renal failure and Non Steroidal Anti-Inflammatory drugs

Introduction: Non Steroidal Anti-Inflammatory (NSAI) drugs, widely used, are prescribed for fever in 25% of the cases. Nephrotoxicity is responsible for 1 to 5% of the causes of acute renal failure (ARF) in children. Hypovolemia or previous renal involvement increase the nephrotoxicity of the NSAI. NSAI drugs induce a renal hypoperfusion by decreasing prostaglandin synthesis, leading to acute tubular necrosis (ATN). They also can cause an immunoallergic reaction responsible for an acute tubulointerstitial nephritis (ATIN).

Observations: We reported 3 cases of severe ARF secondary to a short-course ibuprofen administration at therapeutic level. None of these children had previous renal pathology.

Case 1: Ibuprofen administration in a 4 year-old girl in a context of a viral infection and vomiting. The child presented anuria, with a maximum creatininemia at 850 µmol/l. Dialysis was immediately started. Renal biopsy showed a severe ATIN associated with an ATN. The outcome was not favorable, with the persistence of a chronic renal failure requiring dialysis.

Case 2: Ibuprofen administration in a 8-year-old boy in a context of pleuropneumopathy and vomiting. Maximum creatininemia was 320 µmol/l, diuresis was preserved. A favorable outcome was observed after rehydration and NSAI stop. The final diagnosis was an ATN due to NSAI, but renal biopsy had not been performed.

Case 3: Ibuprofen administration in a 5-year-old boy in a context of pneumopathy and vomiting. The child was anuric, maximum creatininemia was 490 µmol/l. renal biopsy showed an ATIN and acute glomerulonephritis lesions. The outcome was favorable.

Conclusion: NSAI are toxic and can cause severe ARF, particularly in a context of dehydration. Clinical and biological signs are not specific, only renal histology can confirm the renal lesions. Renal biopsy can be discussed for the management of these children. This complication can be prevented, and paracetamol has to be the first antipyretic drug.

P14’: Néphropathie tubulo-interstitielle aigue chez l’enfant: présentation clinique et évolution

Background. La néphropathie tubulo-interstitielle aigue (NTIA) est une cause fréquente d’insuffisance rénale aigue (IRA). Cependant l’étiologie, le traitement et l’évolution chez l’enfant ne sont pas bien connus. Le tableau clinico-biologique est peu spécifique, la confirmation diagnostique est histologique. La place des corticoïdes dans le traitement des NTIA n’est pas bien définie. L’évolution est généralement favorable, mais l’insuffisance rénale chronique est possible. Ce travail décrit les données clinico-biologiques d’une cohorte d’enfants ayant présentés une IRA dont l’exploration par ponction biopsie rénale (PBR) a permis de porter un diagnostic histologique de NTIA.


Résultats : Sur les 306 PBR réalisées pendant cette période, 25 cas (8%) étaient des NTIA. L’âge médian au diagnostic était de 12.9 ans. Le signe clinique le plus fréquent était la douleur abdominale (44%). La médiane de la clairance de la créatinine au diagnostic était de 30ml/min/1,73m². La principale étiologie suspectée était médicamenteuse (32%). Les autres étiologies étaient des néphrites tubulo-interstitielles avec uvéites (TINU syndromes) (28%), des infections (8%) et des toxiques autres que les médicaments (4%). Dans 28% des cas, aucune étiologie n’était retrouvée. Dans la majorité des cas (72%) un traitement par corticoïdes était instauré (1 à 2 mg/kg/jour), à doses dégressives pendant une durée moyenne de 5 mois. Au cours du suivi, 36% des patients ont développé une insuffisance rénale chronique et 12% une hypertension artérielle.

Conclusion : La NTIA est une cause fréquente d’IRA chez l’enfant. Dans notre série, la principale étiologie était médicamenteuse. Le traitement n’est pas bien codifié mais fait souvent appel aux corticoïdes. Le risque d’insuffisance rénale chronique est significatif et justifie un suivi à long terme.

Acute tubulointerstitial nephritis in children: clinical presentations and outcomes

Background: Acute tubulointerstitial nephritis (ATIN) is a frequent cause of acute renal failure (ARF). However etiologies and outcomes in children are not well known. The clinical and biological signs are not specific, so the diagnosis has to be confirmed by renal histology. The indication of corticosteroids is not currently defined. Outcome is usually favorable but a chronic renal failure can occur. This study described the clinical and biological parameters in a cohort of children presenting with ARF due to an ATIN confirmed y a renal biopsy.
Methods: This was a retrospective monocentric study. Children presenting an ATIN confirmed by a renal biopsy between January 2006 and January 2016 in a university hospital (Marseille Timone) were included. Incidence, clinical presentation, cause, treatments and outcome were evaluated for each patient.

Results: 306 renal biopsies were performed during this period, 25 (8%) revealed an ATIN. Median age at the diagnosis was 12.9 years. The most frequent clinical sign was an abdominal pain (44%). Median creatinine clearance at the time of diagnosis was 30 ml/min/1.73 m^2. The main suspected cause was drug toxicity (32%), then TINU syndromes (TubuloInterstitial Nephritis with Uveitis) (28%), infections (8%) and others toxics (4%). No cause was found in 28% of the cases. In most cases (72%), a treatment with corticosteroids was administered (1 to 2 mg/kg/d), with decreasing doses during a mean period of 5 months. During follow-up, 36% of the patients developed chronic renal failure and 12% hypertension.

Conclusion: An ATIN is a frequent cause of ARF in children. In our cohort, the main cause was drug toxicity. The treatment is not well defined but is usually based on corticosteroids. There is a risk of developing chronic renal failure, so a long term follow up is necessary.

P15’: SARS2 mutation as a cause of HUPRA syndrome

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Introduction: The most common renal phenotype of mitochondrial cytopathies is tubulopathy (Fanconi syndrome), but few patients present with nephrotic syndrome or chronic tubulo-interstitial nephritis.

Case report: We report the case of a young boy who presented at the age of 3 years with chronic kidney disease, associated with hypertension, polyuria and polydipsia, failure to thrive and hemolytic anemia requiring repeated RBC transfusions. Hemoglobin electrophoresis was normal and pyruvate kinase and G6PD deficiencies were eliminated. His lymphocyte count showed global lymphopenia, prevailing on CD4+ T lymphocytes and B-lymphocytes. Thrombocytopenia subsequently developed. Renal ultrasound found normal size hyperechoic kidneys. A kidney biopsy was performed and revealed chronic tubulo-interstitial nephritis, with negative immunofluorescence. Ophthalmology examination did not show any sign of retinitis. Brain MRI showed cerebellar atrophy and hyperintensities. His chronic kidney disease progressively worsened, and hemodialysis was started on a central catheter at the age of 5.
A next-generation sequencing panel of ciliary genes failed to detect any pathogenic mutation. Exome sequencing was therefore performed and revealed two heterozygous missense mutations in the SARS2 gene encoding a mitochondrial t-RNA synthetase, along with a hereditary spherocytosis STPB de novo mutation.

Subsequently, he presented several episodes of dyspnea and oxygen-dependency. Echocardiography revealed left ventricular hypertrophy and pulmonary hypertension. Metabolic workup showed elevated serum lactate. He also presented acute neurological signs (hemiparesis, clonic movements) with hyperintensities in basal ganglia on brain MRI, in favour of stroke-like episodes. His overall clinical condition gradually deteriorated, and he died of pulmonary hypertension at the age of 5.

Discussion and conclusion: SARS2 mutations have been previously described in 5 children with a multiorgan disease including HyperUricemia, Pulmonary hypertension, Renal failure in infancy, and Alkalosis, designated as HUPRA syndrome. We suggest targeted screening of SARS2 gene in presence of the combination of these signs or of chronic tubulo-interstitial nephritis of unknown origin in a young child.

P16’: Clinical outcomes in children with Henoch–Schönlein purpura nephritis without crescents

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Introduction: Henoch-Schonlein purpura is the most common vasculitis in children. His long-term prognosis depends on renal involvement. The management of Henoch-Schonlein purpura nephritis (HSPN) remains controversial. This study reports the prognosis of children with HSPN presenting with class 2 ISKDC nephritis.

Methods: All children with HSPN Class 2 diagnosed between 1995 and 2015 in four pediatric nephrology centers were included and clinical and biological data were collected from the medical files. The primary endpoint was the remission of proteinuria defined as a proteinuria <200mg/L.

Results: 92 children were included with a median follow-up time of 36 months. 28% had nephrotic syndrome, 31% proteinuria> 3 g/L, 52% proteinuria between 1 and 3 g/L and 18% proteinuria <1 g/L. 47% received treatment with oral steroids alone, 37% received methylprednisolone pulses followed by oral steroids, 18% have not been treated with steroids. 85% reached remission during follow-up but 12% of them did not maintain complete remission over time so that only 75% remained in complete remission by the end of the follow-up. Univariate analysis found a linear increase of the likelihood of remission with initial proteinuria (p = 0.009). This trend was not found in
the multivariate analysis after adjusting for treatments as patients with higher proteinuria were most often treated with steroids.

**Conclusion:** our study underlines that one fourth of the patients with HSPN class 2 remain proteinuric and thus carry the risk of developing chronic kidney disease on the long term. This finding together with the better outcome of patients treated with steroids is in favor of treating those patients.

**P17’: Hemolytic uremic syndrome associated with *Bordetella pertussis* infection in an infant**

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**Introduction:** Hemolytic uremic syndrome (HUS) has been associated with a number of infectious agents. We report here the case an infant with severe *Bordetella pertussis* infection who developed HUS.

**Case report:** A 2-month-old preterm boy (34 weeks GA) was admitted for cough and fever. Laboratory investigations showed hyperleukocytosis (60x10⁹ cells/L) with lymphocytosis, mildly elevated C reactive protein (32 mg/L) and unremarkable remaining blood parameters. The child was not yet immunized and PCR was positive for *B. pertussis*. He rapidly developed respiratory distress syndrome requiring transient non-invasive ventilation and a macrolide antibiotic. At day 3 after admission, he presented hemolytic anemia with schistocytes, high blood pressure, marked proteinuria and progressive rise of serum creatinine which made us start a diagnostic workup of HUS. Stool culture detected no *Escherichia coli*, and PCR specific for the Shiga toxin genes (stx1, stx2) and the eae gene were negative. Routine complement activation showed no evidence of complement alternative pathway activation (normal C3, C4 and complement factor B levels, transient decreased expression of MCP on peripheral leucocytes, no quantitative deficiency of complement factor H and complement factor I, and no anti-factor H autoantibody). ADAMTS13 activity was within normal range. Severe renal failure led to the initiation of peritoneal dialysis on day 12 after admission. He received eculizumab therapy at days 19, 27, 34 and 48. His renal function gradually improved and dialysis was discontinued at day 37. After 2 months hospitalization the infant was discharged home. Laboratory tests showed normalization of renal function and hematologic values. High blood pressure persisted.

**Discussion/Conclusion:** Five cases of HUS associated with *B. pertussis* infection have been previously described (including one with CFH mutation and one with MCP mutation). Our case suggests a possible direct causal link between pertussis toxins and hemolytic uremic syndrome.
P18': Prenatal hyperechogenic kidneys in a child carrying two NPT2a (SLC34A1) mutations

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Case: we saw the mother of L. during pregnancy because foetal ultrasound (US) showed hyperechogenic kidneys at 22 weeks of gestation. Kidneys were of normal size. Herechogenicity was diffuse and cortico-medullary differentiation was decreased. Amniotic fluid (AF) volume was normal. US performed at 25, 28, 32 and 35 weeks showed similar results (hyperechogenic kidneys of normal size and normal AF). Renal US in parents were normal. L. was born at 38 weeks of amenorrhea. Weight 2960g. Apgar 10-10. At 2.5 months he had an acute pyelonephritis and renal US showed typical aspect of nephrocalcinosis. Biology: Serum creatinin : 22 micromol/L; HCO3-: 21.5 mmol/L; Chloremia : 106mmol/L; Kalemia : 4.6mmol/L; Natremia: 137mmol/L; Magnesemia: 0.75mmol/L; Calcemia: 2.68mmol/L; Ca**:1.44mmol/L; Phophatemia: 1.68mmol/L; Calciuria/creatininuria: 2.7mmol/mmol; Phosphaturia 3.23mmol/L; TmPh/DFG = 2 (Normal at that age: 1.48-3.3); Urinary Na: 20mmol/L; Urinary pH: 7.4; PTH: 5.6ng/L; 25 hydroxyvitD: 47ng/mL; 1.25hydroxyvit D: 155pg/mL

Molecular analysis using next generation sequencing of a targeted exome panel after multiplex amplification (Tub MASTR™) led to the identification of two heterozygous variations in SLC34A1 (NaPiIIa): c.[644+1G>A(;)1174G>A] p.[(?)(;)(Asp392Asn)]. The first affects splicing and has been reported previously, the second, not described, is absent in ExAC, predicted to be deleterious by in silico programs, and might also affect splicing.

Discussion: Biallelic mutations in SLC34A1 have been reported in association with Fanconi Syndrome (Magen et al) and with idiopathic infantile hypercalcemia type 2 (Schlingmann et al). The features presented by our case are fitting with idiopathic infantile hypercalcemia. However, to our knowledge, it is the first case reported with prenatal hyperechogenic kidneys. Foetal levels of calcium and phosphate are maintained higher than the maternal levels, due to placental active transport. 1,25(OH)2D level is lower in the foetus than that in the mother. The presence of antenatal nephrocalcinosis suggests a dysregulation of foetal phosphocalcic metabolism. Further studies will be necessary to understand the physiopathology.

P19': Can Rituximab help sparing steroids in pediatric patients with severe Lupus Nephritis?

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**Introduction:** Cyclophosphamide or Mycophenolate Mofetil (MMF) with prednisolone is the treatment of reference of severe lupus nephritis. Rituximab (RTX) failed to improve outcome when associated with MMF and corticosteroids. However, recent data suggest that RTX may have steroid sparing beneficial effect with similar efficiency as conventional regimen. We report our experience of the use of RTX in lupus nephritis in children.

**Material and methods:** All patients from 2 centers treated by RTX for a first flare of LN class III to V were included. Treatment associated methylprednisolone pulse (500 mg/m\(^2\)) followed by RTX (1000 mg/1.73m\(^2\)) at day 1 and 15 and MMF (1200 mg/m\(^2\)/day). Prednisolone tapering and withdrawal was left to the discretion of physicians. Complete remission (CR) was defined as Pu/creat <50mg/mmol and normal serum creatinine and partial remission (PR) as Pu/creat <300mg/mmol and <15% rise of serum creatinine over baseline.

**Results:** Twelve patients with biopsy proven LN (7 class IV, 1 class III, 3 class IV+V, and 1 class III+V) were included. Median age was 13.7 years [12.5-15.1] and median follow-up 17.1 [9.5-31.5] months. Median proteinuria was 320 [110-660] mg/mmol and median eGFR was 76.0 [59.7-81.8] mL/min/1.73m\(^2\).

Median CD20 depletion duration was 9.5 [6.8-10.5] months. At 6 months, 4 patients required another RTX infusion. Prednisolone was rapidly tapered down with a median dose of 0.33 [0.19-0.44], 0.10 [0.08-0.17], 0.0 [0.0-0.05] mg/kg at 3, 6 and 12 months respectively. At 3 months, 3 patients achieved CR and 6 PR. At 6 months and 12 months all patients achieved remission (8 CR and 3PR at M6 and 7 CR and 1PR at M12) and none relapsed during follow-up. Four infectious complications were observed (1 septic shock, 1 pneumonia, 2 varicella).

**Conclusion:** Combining RTX and MMF with a rapid decrease of steroids seems efficient in severe lupus nephritis. The ability of RTX to allow complete steroid avoidance warrants further investigation in children.

**P20':** Post-traumatic bilateral ischemic infarction and renal failure without vascular lesions in a 12 year-old girl – The pathogenic role of vasospasms

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**Introduction:** Post-traumatic renal failure, although rare in paediatrics, is often due to severe trauma with post-ischemic renal infarct, caused by identified lesions such as aortic or renal artery dissection, bilateral renal vessels thrombosis, haemorrhagic shock or crush syndrome with rhabdomyolysis.

**Case report:** We report on a 12 year-old girl with acute anuric renal failure requiring hemodialysis after severe abdominal trauma. A CT-scan performed immediately after
initial presentation revealed a haemoperitoneum without pneumoperitoneum, an increase of pancreatic head size, a heterogeneous and bilateral diminished enhancement of the kidney, indicating a bilateral renal necrosis. A second CT-scan was performed on day 7, showing a bilateral pleural, pericardial and peritoneal effusion and persistence of lesions compatible with infarction in multiple zones of the renal parenchyma, with a patchy distribution. No artery dissection and no thrombosis were identified. A Doppler-sonography confirmed the non-interruption of blood flow, especially at the renal artery ostium and renal biopsy showed typical lesions of diffuse bilateral renal ischemic necrosis. The main hypothesis is a severe bilateral arterial vasospasm after a blunt abdominal trauma, who was presumed in an others cases. The vasospasm of small vessels and liberation of toxin with consequent endothelial injury seems to be the initiating event in the process of cortical necrosis. The patient recovered only partially with persisting chronic renal failure.

**P21’: A rare cause of hyperkalemia in infancy**

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**Introduction:** The diagnosis of Gordon syndrome or pseudohypoaldosteronism type II is often made in the work-up of high blood pressure. However, in young children, the presentation of this disease may be different and isolated hyperkalemia should alert us.

**Case report:** A 13 month-old girl (7.1 kgs, 73 cm), with a recent diagnosis of cow’s milk protein allergy with failure to thrive and diarrhea, was referred to our center for incidental finding of hyperkalemia (K+: 7.5 mmol/l), and hyperchloremic metabolic acidosis (HCO3-: 15 mmol/l). Glomerular filtration rate was normal. In vitro hemolysis was ruled out. The renin and aldosterone plasmatic levels were below the threshold of detection. Clinical examination and psychomotor development were normal as well as blood pressure (90/55 mmHg). After the beginning of oral thiazide, her serum electrolytes promptly normalized. A mutation in the CUL3 gene was identified.

**Discussion:** 4 genes are responsible for Gordon syndrome: WNK1, WNK4, KLHL3 and CUL3 (Boyden LM and al. Nature. 2012 Jan). The last two encode the Kelch-like 3 and cullin-3 proteins, which regulate the ubiquitination and degradation of WNK kinases. (Shibata S. and al., Proc Natl Acad Sci USA. 2013 May; Louis-Dit-Picard H. and al. Nat Genet. 2012 Mar). Inheritance of CUL3 mutations is in an autosomal dominant pattern and identified variants are mostly de novo mutations. The associated phenotype is severe with early presentation (form with highest blood pressure and hyperkalemia). It can be also associated with dental abnormalities and growth retardation. (Bruel A. and al., Arch Pediatr. 2016 Aug)

**Conclusion:** The early diagnosis of pseudo-hypoaldosteronism type II would be important to prevent the complications of the high blood pressure, and failure to thrive.
Therefore, in the presence of hyperkalemic metabolic acidosis, the diagnosis of Gordon syndrome should be considered despite the rarity of the disease.

**P22’**: Rituximab to maintain remission in a granulomatosis with polyangiitis with severe glomerulonephritis

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**Introduction**: Cyclophosphamide (CYC) and non-selective immunosuppressive agents such as steroids and Azathioprine (AZA) are associated with substantial toxicity and sometimes fail to achieve and sustain remission in Granulomatosis with Polyangiitis (GPA). The use of Rituximab (RTX) in adults with GPA seems to have positive results. Still the experience in children is limited. We describe a child with GPA, both severe renal and respiratory involvement, with clinical remission while treated by RTX.

**Case report**: A 7-year-old caucasian girl was diagnosed with GPA based on the combination of purpura, alveolar haemorrhage, nasal granulomas, acute renal failure with serum creatinine (SC) reaching 122μmol/L, nephrotic syndrome and necrotizing glomerulonephritis and high c-Anti-Neutrophil Cytoplasmic Antibodies (cANCA) levels. Induction therapy combined 3 daily steroid pulses and one CYC pulse, repeated 15 days later as the SC level remained around 100 μmol/L. Cumulative CYC dose was 55 mg/kg. RTX maintenance therapy started on day 30 at a single dose of 375 mg/m² associated with AZA and 6 month-tapering oral steroids. Complete B-cell depletion was obtained at day 20 after RTX injection and CD19 levels, regularly screened in order to detect B-cell reconstitution and indicate the second injection, were still negative after 6 months. cANCA titers decreased, SC levels fell within the normal range and respiratory symptoms improved. No infection was noticed but serum immunoglobulin levels showed a significant gradual decrease.

**Discussion**: B-lymphocytes have been involved in GPA pathogenesis, their depletion was indicated primarily as salvage therapy for refractory disease. Few data report RTX use in pediatric patients, however, several controlled trials showed its efficacy in both induction and maintenance remission in adults. In recent trials, RTX is not inferior to CYC for remission induction and might be superior in relapsing disease. Most clinical studies and pediatric case reports have emphasized the low incidence of severe side-effects from RTX treatment.

**Conclusion**: This case shows that RTX is a good tool in controlling a complicated GPA and sparing steroids and CYC, but we need further recoil to assess its long-term efficacy and safety through proper trials in pediatric population.
**P23’: Sodium and potassium balances evolution in children with autism treated with bumetanide.**

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**Introduction.** Autism is a developmental disorder associated with social disability, communication impairments, repetitive behaviors and restricted interests. Many factors seem to contribute to autism development, and multiple causes have been linked to autism, but there is no specific treatment available. Recently bumetanide has been described to improve behavior of autistic patients through the modification of GABAergic neurons metabolism. While prospective studies are ongoing, little is known about the actual impact of such a treatment in children with no cardiac, kidney or lung diseases.

**Objective.** The aim of this study was to assess the impact of bumetanide on sodium and potassium balances, and on plasmatic renine and aldosterone levels in children with autism.

**Design.** This study was monocentric, descriptive and prospective. Inclusion criteria were: confirmed autism, bumetanide indication (by the patient’s referent physician), ability to collect 24h urines, informed consent of the parents. Exclusion criteria were: any cardiac, renal or lung underlying disease, administration of other treatment interfering with bumetanide. Patients were prospectively studied during the first 20 days of bumetanide treatment with clinical and biological evaluation including daily sodium and potassium intake, 24h urine collection and blood samples for potassium, renin and aldosterone level determination.

**Results.** Sodium balance became progressively negative with a maximum at D10 (-98mmol/24h) and progressively switched to positive levels at D20. The nadir of potassium balance was D2, with a progressive increase and a maximum at D20. Plasmatic potassium levels were the lowest at D5 (3.25mmol/L). Plasmatic renin and aldosterone levels increased with a peak at D5 and D10 respectively.

**Conclusion.** These results confirmed in autistic patients data published in other populations. Such results can help physician to safely use bumetanide in these children. In addition these results suggest a strategy using increasing doses may be a solution in order to avoid hypokalemia.

**P24’: Steroid treatment in children with IgA nephropathy**

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**Introduction:** IgA nephropathy (IgAN) is one of the most common primary glomerulonephritis in children and adolescents worldwide and have long considered as a relatively benign disease. However, a 20 year-long study cohort showed that pediatric outcome is as serious as in adults. We report a retrospective pediatric cohort of IgAN and describe clinical presentation, histopathologic lesions and treatment. Our goal was to evaluate the efficacy of steroids on proteinuria and estimated glomerular filtration rate (eGFR).

**Methods:** We reviewed the charts of 83 consecutive children and adolescents from Necker hospital and Robert-Debré Hospital diagnosed between 1990 to 2015 with primary IgAN after a renal biopsy. The cohort was divided into two groups: C1, treated with both immunosuppressive regimen (Steroid therapy +/- Endoxan) and supportive care (renin angiotensin system blockade) and C2, treated only with supportive care. Proteinuria and eGFR was evaluated between the onset of disease (M0) and 6 months later (M6).

**Results:** 83 children were enrolled in this study. At the onset, 20 patients (24.1%) presented with acute renal failure, and 8 (9.6%) with nephrotic syndrome. 52 patients (62.7%) constituted the C1 group, and 20 patients (24.1%) constituted the C2 group. 11 patients (13.2%) were not given any drug. eGFR in C1 group had significantly improved between M0 and M6 (93.6 (66.3-119,2) vs 114.7 (97.7-137) ml/min/1.73m², p=0.0065). Proteinuria had also significantly decreased (0.16 (0.1-0.42) vs 0.03 (0.018-0.06) g/mmol creat, p=0.0001). In the C2 group, eGFR and proteinuria was comparable. Multivariate analysis showed endocapillary proliferation significantly associated with the decision to treat with immunosuppressive agents (78% vs 38.89%, p=0.0037).

**Conclusions:** Immunosuppressive treatment, especially steroid therapy, for children with severe IgAN, significantly reduced proteinuria and improved eGFR level after 6 months of treatment. Endocapillary proliferation seems to be a good marker of steroid sensitivity in IgAN.

**P25’:** Insuffisance rénale aigue avec microangiopathie thrombotique diffuse révélant un syndrome de CASTLEMAN

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**Introduction:** Le syndrome de Castleman est un syndrome lymphoprolifératif atypique, rarement révélé par une insuffisance rénale aigue.
**Observation:** Un adolescent de 17 ans, a présenté une insuffisance rénale aigue, au décours d’une gastroentérite avec prise d’ibuprofène. Son bilan initial montrait une anémie normocytaire arégénérative, des plaquettes à 165 000/mm3, une VS à 52 mm, schizocytes et LDH normaux, une créatinine à 181 micromol/l, urée à 23 mmol/l. Bilan immun normal. L’aggravation de l’insuffisance rénale, associée à un syndrome oedémateux majeur, a conduit à la réalisation d’une ponction biopsie rénale révélant des lésions de microangiopathie sthrombotiques diffuses. L’hypothèse d’un syndrome de Castleman a été évoquée et prouvée par un bilan d’extension scannographique (épanchement pleural Gauche, péricardite, hépatosplénomégalie et polyadénopathies cervicales, axillaires, latéroaortique gauche) et une biopsie ganglionnaire cervicale Gauche. Sur le plan étiologique, PCR HHV8 négative, sérologie HIV négative, activité ADAMTS13 diminué à 28% compatible avec un SHU. PCR sanguine à EBV positive à 900 copies à l’entrée.

**Prise en charge thérapeutique et évolution:** La réalisation d’un bolus de Solumédrol couplé à une dose d’Etoposide à 100 mg/m2, puis relayé par une corticothérapie à 1mg/kg/jour et 4 injections de Rituximab à 375 mg/m2/hebdomadaire ont permis une amélioration de la fonction rénale. Les deux principales complications ont été une poussée d’HTA avec PRESS syndrome lorsque la créatinine était à 330 micromol/l à J21 d’hospitalisation. A 8 mois du diagnostic, la créatinine est à 88 micromol/l et la récupération du PRESS Syndrome complète. L’arrêt complet des corticoïdes à 6 mois se maintient sans rechute à ce jour.

**Conclusion:** La présence d’une Microangiopathie thrombotique diffuse sur une Biopsie rénale doit faire évoquer une maladie de Castleman. Le diagnostic de certitude se fait par une biopsie d’un ganglion atteint dont la localisation est guidée par un scanner avant mise en route de la corticothérapie.

**Accute renal failure with diffuse thrombotic microangiopathy revealing a castelman syndrome.**

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**Introduction:** Castleman’s syndrome is an atypical lymphoproliferative syndrome, rarely revealed by acute renal failure.

**Observation:** A 17 years old teenager, presented an acute renal failure, after taking ibuprofen while suffering from gastroenteritis. His initial blood tests showed normocytic aregenerative anemia ; platelets : 165,000/mm3 ; schistocytes; sed rate : 52 mm ; normal LDH level ; creatinine :181 imol/L ; urea : 23 mmol/L ; normal autoimmune tests. In view of a major edematous syndrome and the worsened renal failure, we performed a renal biopsy revealing lesions of diffuse thrombotic microangiopathy. The diagnosis of Castleman’s syndrome was discussed and demonstrated by further scannographic evaluation (Left--sided pleural effusion, pericarditis,
hepatosplenomegaly cervical, axillary and left latero---aortic polyadenopathy) and a left cervical lymph node biopsy. Concerning etiology, HHV8 PCR and HIV serology were negative. ADAMTS 13 activity decreased to 28% which was compatible with HUS. The EBV blood PCR was positive up to 900 copies.

**Therapeutic management and development:** A methylprednisolone pulse associated with a injection of etoposide at 100 mg/m², then relayed by corticosteroid therapy at 1mg/ kg/day and 4 injections of rituximab at 375 mg/m²/week have improved the renal function. The two main complications were an hypertensive crisis with PRES syndrome when creatinine level was up to 330 µmol/L after 21 days in hospital. Eight months after diagnosis, the creatinine level is 88 µmol/L and he achieved Full recovery from his PRES Syndrome. The corticosteroids were stopped after 6 months without relapses up to this day.

**Conclusion:** The presence of diffuse Thrombotic microangiopathy on a renal biopsy should suggest Castleman disease. Definitive diagnosis is made after biopsy of an affected lymph node located by a scanner before initiation of corticosteroid therapy.