TRAINING REPORT

Pediatric Nephrology Department of Hôpital Femme Mère Enfant (HFME) Lyon, France

From November 2, 2015 to April 30, 2016

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ACKNOWLEDGMENTS

We would first like to thank Mr. Pierre COCHAT, chief of the Pediatric Nephrology department at the Néphrogones Reference Center for rare renal diseases at Hôpital Femme Mère Enfant (HFME) in Lyon for having welcomed us as student interns (FFI).

Thank you to Professor Marc NICOLINO, coordinator of the DES/DESC in pediatrics at HFME, who was charged with the pedagogical monitoring of our training.

We must also thank all of Prof. COCHAT's colleagues as well as all of the personnel of his unit for everything that they did on their part.

We must not forget to acknowledge IPNA (Association Internationale de Néphrologie Pédiatrique/International Association of Pediatric Nephrology) that supported us financially throughout this internship.

Thanks also to the assembly of teachers from DES in Pediatrics from the Medical School of Abidjan, especially to the Director, Professor OULAI Soumahoro, for having provided a favorable recommendation during this internship.

Finally, we especially thank Professor ADONIS-KOFFY Laurence who recommended us to Professor Pierre COCHAT.

INTRODUCTION

As part of the agreement between Université Claude Bernard Lyon 1 and the Centre Hospitalier de Yopougon and under the financial coverage of Association Internationale de Néphrologie Pédiatrique (IPNA), we benefited from a medical internship as Medical Interns (FFI) in the pediatric nephrology, dermatology, and rheumatology department at Hôpital Femme Mère Enfant in Lyon. This internship that took place under the supervision of the department head, Professor Pierre COCHAT, was part of the DFMS program (Diplôme de formation spécialisée/Diploma of Specialized Training).

The main objective was to be able – at the end of this internship – to treat specific problems of children in Côte d'Ivoire who are afflicted with renal diseases. In this country, there is already one pediatric nephrology department under the direction of Professor ADONIS-KOFFY Laurence in which we got to know this subspecialty.

During the six-month period between November 2, 2015 and April 30, 2016, our training was both theoretical and practical.

I- PRESENTATION OF THE INTERNSHIP SITE

1- Hôpital Femme Mère Enfant (HFME) of Lyon

HFME is one of the hubs of the university medical center of Lyon. Linked to the hospital group is the Hospices Civils de Lyon (HCL), which is located in the municipality of Bron.

My internship took place in the pediatric nephrology, dermatology, and rheumatology department that shares the 5th floor of this building with the pediatric neurology department.

2- The pediatric nephrology, dermatology, and rheumatology department

This department is directed by Professor Pierre COCHAT. Called "Néphrogones," the "Pediatric Nephrology" hub is the reference center for rare childhood renal diseases. This center has 10 strategic foci:

1. To study the epidemiology of rare diseases
2. To identify the specific features of rare diseases
3. To develop information for sick individuals, health professionals, and the general public
4. To train health professionals to better identify rare diseases
5. To organize testing and access to diagnostic tests
6. To improve access to treatment as well as to quality of care
7. To continue the effort in support of orphan medicinal products
8. To respond to specific support needs of people afflicted with rare diseases
9. To promote research on rare diseases
10. To develop national and European partnerships

The medical team of the department is made up of:

- Mr. Pierre Cochat, university professor-hospital practitioner (PU-PH), director of the department
- Mrs. Justine Bacchetta, university hospital practitioner (PHU) in pediatric nephrology
- Mrs. Odile Basmaison, hospital practitioner in pediatric nephrology
- Mrs. Aurélia Bertholet-Thomas, hospital practitioner in pediatric nephrology
- Mrs. Laurence Dubourg, university lecturer- hospital practitioner (MCU-PH) intervener for evaluation of renal function
- Mrs. Anne-Laure Leclerc, hospital practitioner in pediatric nephrology
- Mrs. Sandrine Lemoine, hospital practitioner in adult nephrology
- Mr. Bruno Ranchin, hospital practitioner in pediatric nephrology.

The thematic research specifics of this center focuses on:

- Lithiasis nephrocalcinosis, calcium phosphate metabolism, tubular exploration,
- cystinosis,
- lupus,
- hemolytic uremic syndrome,
- transplant (In 2015, the center conducted 19 renal grafts of which 3 were double liver/kidney grafts), peritoneal dialysis (PD), hemodialysis (HD)

The medical operations of this department recognize several units:

- **The conventional hospital** in which children with kidney, skin, or rheumatological diseases are admitted requiring hospitalization (419 hospital stays in 2015). These children are taken care of at the medical level by residents and interns (FFI) who give advice under the supervision of the attending physician (CCA). Treatment is carried out by a nursing team that also takes care of the pediatric neurology department.

- **The hospital's day clinic** in which consultations and hospitalizations of a few hours (less than 24 hours) are scheduled for children being cared for in nephrology, rheumatology, and dermatology. During the year 2015, 440 stays were recorded in this department.

  Consultations relate to children requiring regular weekly monitoring: one, two, or three times per week (children with chronic peritoneal dialysis, monitoring of grafts, etc.) but also post-hospitalization monitoring of some children.

  Hospitalizations are noted:

  - As part of exploration (biological observation assessment, evaluation of renal function by iohexol or inulin clearance, determination of the kinetics of certain medications, notably immunosuppressant: the AUC of CellCept, for example),
  - As part of parenteral therapeutics requiring a specific observation (perfusion of immunoglobulin, perfusion of Rituximab, perfusion of zoledronic acid or Zometa*, etc.)

  Within the hospital's day clinic, children are cared for from the moment of their arrival by the resident who conducts a clinical evaluation and by the nursing staff in the case of a biological test. Based on the clinical and paraclinical results, the resident can then authorize the nurses to carry out the prescribed therapy.

  The resident's work is overseen by a senior nephrologist, on one hand, (professor and hospital practitioner) and by a rheumatologist, on the other hand (university practitioner, hospital practitioner). It is these senior staff who are directly involved with consultations at the hospital's day clinic.

  Every Friday afternoon, a medical assembly is held touching upon the whole of the patients visited throughout the course of the week. Participants are chiefly all of the intervening physicians within the day clinic, the ATTENDING PHYSICIAN, and the

assigned resident. But this exchange is also open to other residents depending upon their availability.

- **The dialyses unit** is the site in which hemodialysis sessions (HD) of children are conducted (HD) in accordance with a regular schedule. This unit is under the supervision of a hospital practitioner aided in his tasks by a resident.
- **Pediatric nephrology consultation activity** mainly occurs at the specialized pediatric consultations hub on the 4th floor. The 2015 activity report noted 3,000 consultations.

II- OUR ACTIVITIES

During this period, our practical training occurred in consultation with the relevant medical specialty, but also in the conventional hospital where we worked in collaboration with 5 French residents and one Spanish (FFI) medical intern who was also in training. We also received theoretical training.

1- In the conventional hospital

Our activities began with a meeting at 8:45 a.m. on Mondays and at 9:00 a.m. on other days during which the nurses accompanied by their aids briefed the medical team on the health condition of hospitalized children who had been under their observation throughout the night. During these 15-30 minutes of dialogue, a senior physician (university professor/hospital practitioner or hospital practitioner) as well as the attending physician supervise and give instructions to the residents (generally two) in charge of the children throughout the day. This is when possible decisions pertaining to patient release are made.

Then, accompanied by medical students, residents examine the children under their charge and research potential information that might aid in a better diagnostic approach or care of children.

The whole of these elements is noted in the patient's electronic record accessible through the software program, "EASILY." The instructions are carried out and treatments are updated on another program called "CRISTALNET-OPIUM." Afterward, in the middle of the day, generally around noon, we have the intervention of a senior physician, most often the attending physician, who checks and adjusts prescriptions as well as the proper implementation of instructions. Decisions regarding conditional release awaiting satisfactory exam results are then confirmed or overturned. These releases are then prepared by the resident who is still under the supervision of the attending physician.

There were several idiosyncrasies (especially on Mondays). We noted the presence of the entire medical staff 15 minutes before the dialogue session with the nurses. This lapse of time gave the senior physician and the resident the weekend to make an assessment on the whole of the patients under their charge.

Thursdays, a medical assembly of approximately 1.5 hours in length is conducted in the presence of the department head, the hospital practitioner, the attending physician, the residents of the conventional hospital, as well as the externs. Residents fully present each of the children under hospital care, referring to acknowledged problems so that decisions regarding them can be made. Secondarily, instructions are carried out by the residents.

2- Consultation

Consultation was mainly a place of observation. For a given pattern of consultation, it consisted of following the process from the examination to the diagnostic exam by way of the physical exam. It also served to understand the proceedings of the clinical and paraclinical monitoring of a known renal illness and to take care of a child referred for a recently-

discovered renal pathology: it consists of conducting a wider inquiry that incorporates family and personal histories by attempting to construct a family tree.

The consultation was conducted by a pediatric nephrology physician. Note that we still had the authorization to examine patients during the course of the consultation.

This activity was very valuable for it allowed a closer exchange on subjects not necessarily common in hospitalization. We could thus discover variable ways from one intervener to another to approach different medical problems allowing us to expand our own idea without deviation from the norm with regard to conduct in response to patient complaints. And finally, and most importantly, it allowed us to participate more than once in Professor COCHAT's consultations, which taught us a great deal.

3- Theoretical Training

- **In the hospital setting**

We attended courses scheduled every Thursday on the department's most common pathologies, relevant treatments (corticotherapy, immunotherapy, etc.), studies (clearance studies, for example) concerning pediatric nephrology, but also courses on practical pediatric rheumatology and dermatology. The sole purpose was to give residents the basic means permitting them to progressively acquire autonomy in patient care.

Furthermore, we participated in multidisciplinary meetings where one of our patients presented an extra-renal problem necessitating the intervention of another specialist (infectiology, rheumatology, anatomopathology). We exhibited the clinical picture of the patient while outlining the problem. That generated a discussion in which each of us could give his/her opinion. Ultimately, recommendations were given to the interveners responsible for the patient in the form of a synthesis.

Finally, we appreciated attending the meetings of the Multidisciplinary Center of Prenatal Diagnostics with Dr. Aurélia Bertholet-Thomas on three occasions, one of the hospital practitioners of the department. Throughout these meetings, we noted the presence of many specialists (pediatric nephrologists, pediatric cardiologist[s], pediatric radiologists, pediatric surgeons, etc.). The goal of these meetings was to present cases of antenatal diagnosis (AND) in order to put parents in touch with the specialist in question (this was the most common case for pediatric nephrology) or to grant the authorization of a request for a medically-induced termination of pregnancy (ITOP) in the event of non-viability of the fetus bearing a deformity.

- **Outside of the hospital setting**

We participated in the 31st Annual Francophone Convention of Pediatric Nephrology in Strasbourg from December 3-5, 2015.

We also took part in the Inter-University Diploma of Pediatric Nephrology (DIU) that occurred in 4 sessions of which each session includes 32 hours of courses spread out over 4 days (from Tuesday to Friday):

- The first session was in Nice from December 15-18, 2015
- The second in Paris from January 19-22, 2016
- The third in Montpellier from March 15-18, 2016
- The fourth scheduled for Lyon from May 10-13, 2016

A total of 100 classes of which 74 were already waived while awaiting the final session.

For the validation of this DIU, an essay is scheduled for June 21, 2016. It occurs in two parts: a 3-hour theoretical part involving three major issues and three clinical cases followed the same day by a 10-minute PowerPoint presentation with 5 minutes of questions from the Jury.

Our thesis topic concerns “kidney damage in patients with Trisomy 21 (Down’s Syndrome)”. This work relates to the cases of CAKUT (Congenital Abnormalities of the Kidney and Urinary Tract) in children monitored in the pediatric nephrology department of Hôpital Femme Mère Enfant in Lyon during the period from January 2010 to April 2016.

And via a lit review, we are going to insist on the diversity of kidney damage throughout this chromosomic aberration, their possible evolution toward chronic kidney disease and thus the necessity to look for them in order to propose adapted monitoring and care, especially when renal function is compromised.

III- EXAMPLES OF PATHOLOGIES AND CLINICAL CASES ENCOUNTERED

A- During Hospitalization

We encountered varied pathologies sometimes having no relationship with the department as part of the winter plan (bronchiolitis, asthma attack, osteosarcoma, dysimmune syndrome, etc.). We will list below for you a few of the educational clinical pictures for which we were responsible:

1. Fever during hemodialysis

This pertains to children referred to the dialysis unit for fever. In general, with a biological statement that is already collected and bi-antibiotic therapy targeted for staphylococcal in progress. This might, in fact, be real sepsis or only an intercurrent infection (influenza) in which case the antibiotics are halted in order to confirm the results.

2. Post-kidney/liver transplant monitoring with Type I hyperoxaluria

Hyperoxaluria is a rare disorder of the metabolism of the glyoxylate due to a hepatic enzyme deficit. It is a genetic disease of which there are three types as per the enzyme in question. Type I is a L-alanine:glyoxylate aminotransferase deficit. The clinical presentation is nephrolithiasis that can result in nephrocalcinosis. Progression occurs gradually toward end-stage renal failure (ERF). A double liver/kidney transplant is the last resort. Within this context, a child has been admitted into the hospital for post-operative care after a brief stay in intensive care.

Within this specific context, we noticed complications, particularly a biloma having promoted a recurring aseptic pleurisy despite several drain punctures. A transfer to intensive care for better treatment was necessary.

3. Renal puncture biopsy (RPB) of an original kidney

This RPB was completed within the diagnostic framework of Lupus nephritis in a patient suffering with systemic lupus who presented proteinuria.

1. Renal puncture biopsy of a graft

Two specific cases were presented:

- A systematic RPB at 3 months from the graft in a patient suffering from IgA nephropathy on a rheumatoid purpura. It served to research possible drug-induced lesions.
- The second RPB is that of a patient presenting an elevated level of creatinine on a graft completed within 2 years in the context of renal coloboma syndrome. It concerns a genetic anomaly leading to dysplasia of the optic nerve and renal hypodysplasia. This puncture permits the diagnosis of an acute cellular rejection. This was a case that posed a care issue for we noted several previous rejection episodes of which the last one from one month prior had been treated with boluses of corticoids and with thymoglobulin drips.

2. **Recurring peritonitis on catheter within the framework of anephria with Finnish Nephrotic Syndrome**

Finnish Nephrotic Syndrome is a congenital nephrotic syndrome that does not respond to any medicinal treatment. Renal grafting is the only means to definitively interrupt massive proteinuria. Unilateral nephrectomy, or better, bilateral nephrectomy is an expected while awaiting transplant.

The child that we cared for suffered a bilateral nephrectomy and thus was in iterative peritoneal dialysis (PD). In this context, he presented the 4th relapse of peritonitis. This consisted of multibacterian peritonitis (*Serratia marcescens, Citrobacter Freundii,* and *Klebsiella pneumoniae*). Progress was favorable under antibiotic treatment lead by antibiogram. But facing the frequency of infectious episodes estimated at one per month, the specific nature of *serratia marescens* (biofilm producer), there was a discussion regarding removal of the peritoneal catheter followed by an interim placing in hemodialysis while awaiting a new positioning of the peritoneal catheter.

3. **Therapeutic Non-compliance of a child in end-stage renal failure (ERF) with nephronophthisis having two transplant failures and placement on peritoneal dialysis (PD)**

Nephronophthisis is a chronic tubulo-interstitial nephropathy that progresses toward end-stage renal failure.

Our patient having had two graft failures was awaiting another one and received iterative peritoneal dialysis. Besides medications, there was a diet and lifestyle regimen that was not respected despite the intervention of his family. The clinical result was Edematous syndrome.

It is within this context that hospitalization was recommended not only for control of the regimen, but also for a child psychiatry consultation.

4. **Mycoplasmal pneumonia in a renal graft with steroid-resistant nephrotic syndrome**

Immunosuppressant treatment of grafts exposes them to risk of opportunistic infection. It is within this framework that an adolescent presented with acute respiratory syndrome. PCR positive for Mycoplasma pneumoniae revealed mycoplasmal pneumonia. We note that in the diagnostic immediacy of this patient, a comprehensive evaluation was completed, in particular a bronchoalveolar lavage under general anesthesia. The patient progressed well with macrolide.

5. **Post-Chemotherapy Nephropathy for osteosarcoma of the hip**

For the treatment of osteosarcoma of the hip, a patient was put under chemotherapy containing ifosfamide (nephrotoxic). One month after stopping therapy, proteinuria and worsening of renal failure persisted. The RPB noted severe lesions of tubular necrosis and of tubulite. He thus received three bolus of Solumedrol (Cortisone).

B- In consultation

We are simply going to briefly describe a few pathologies encountered during consultation to which we were not accustomed.

Hypercalciuria with DENT syndrome

DENT syndrome is a proximal tubular nephropathy of genetic origin. It is characterized by a proteinuria of low molecular weight, hypercalciuria, nephrolithiasis, and nephrocalcinosis with a progressive development toward renal failure. It is often exacerbated by rickets.

1. **BOR Syndrome**

Branchio-oto-renal (BOR) syndrome is an autosomal dominant genetic disease. It is characterized by:

- Atrial damage: anomaly of the outer ear (atresia or stenosis of the canal, pre-atrial opening) and deafness of perception or transmission
- A cyst or a fistula of the gill arches
- An anomaly of the kidneys going from hypoplasia renal agenesis.

2. **Bartter Syndrome and Gitelman Syndrome**

Bartter Syndrome is a hereditary tubular nephropathy that can appear at any age (prenatal, neonatal, childhood, adolescence, adult). This renal anomaly causes hypokalemic alkalosis associated with an elevated rate of renin and aldosterone with decreased blood pressure and vascular resistance to angiotensin II. The classic form manifests itself in polyuro-polydypsic syndrome, chronic dehydration, and growth retardation.

Gitelman Syndrome is also a hereditary tubular nephropathy causing hypokalemic alkalosis associated with significant hypomagnesium. It most often begins after age 6. It manifests itself in temporary periods of muscular weakness with tetany accompanied with abdominal pains, vomiting, and fever.

3. **Cystinuria**

Cystinuria is a dominant or recessive genetically-transmitted anomaly of the transport of amino acids in the renal tubule. It is characterized by the recurring formation of cystine

kidney stones. It develops at any age, but renal colics due to cystine stones appear generally during the first 20 years (on average around 15 years).

4. **Fanconi Syndrome**

This is a genetic disease characterized by a generalized proximal tubular anomaly. It manifests itself at any age. For children, symptoms are polyuria, polydipsia, rickets, or stunted growth.

5. **Nephronophthisis**

Nephronophthisis is a chronic tubulo-interstitial nephropathy leading to end-stage renal failure at around age 15. It manifests itself clinically after the age of 2 by disruptions in concentration of urine with polyuria going hand in hand with polydipsia, a decrease in growth, and a progressive deterioration of kidney function without signs of glomerular damage.

6. **Nail Patella Syndrome**

Nail Patella Syndrome is a hereditary onycho-osteodysplasia. It is dysplasia of the nails with a triangular shape, hypoplastic or missing kneecaps, exostoses of the iliac wings (iliac horns), dysplasia of the elbows sometimes with ocular damage (glaucoma, ocular hypertension...) and deafness. Nephropathy is observed in one-third to one-half of cases. It leads to proteinuria, sometimes accompanied by nephrotic syndrome, hematuria, and high blood pressure.

CONCLUSION

In the course of this internship, we had a very enriching experience both medically and personally. We discovered the truth about the diversity of renal pathology in children outside of what is found in medical books. We worked with competent specialists who were available

and enthusiastic to share their medical knowledge. We valued the refined techniques of conducting renal biopsy punctures in ideal conditions. We were even able to attend in close proximity the surgical act of a renal transplant.

It would thus be desirable to continue these exchanges between the pediatric nephrology department of Lyon and the pediatric nephrology unit of Abidjan over a long period of time. In this way, this subspecialty will undoubtedly advance without being tarnished by the disparity of the medical and technical plateau that exists between HFME of Lyon and the CHU of Yopougon.

INTERNSHIP DIRECTOR	**MEDICAL MONITORING AGENT**
Professor Pierre COCHAT	Professor Marc NICOLINO