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ABSTRACTS

INTRA INDIVIDUAL VARIABILITY OF BLOOD PRESSURE IN HEALTHY ADULTS AND CHILDREN.

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Intra individual blood pressure (BP) and heart rate variations and their possible correlation with sex and age were evaluated in 271 healthy adults, adolescents and children divided into equivalent groups of both sexes.
BP and heart rate were measured every minute during 14 minutes with an automatic device using the oscillometric method. A second measurement session was repeated two weeks later. On most patients, a decrease of BP was during the first minutes towards a point of relative stability, which is reached after the eight measurement. Mean differences between the first and the fourteenth minutes was about 12 mm Hg for systolic BP and 18 mm Hg for diastolic BP. The mean values of the 14 determinations on day I and day 15 showed a significant correlation ($r = 0.65$ to $r = 0.75$) according to different groups. The variability index within one subject was not different in children, in adolescents and in adult groups. A comparison of the variability indices observed on day I and day 15 showed a significant correlation only for systolic BP in male and for heart rate in female subjects. Reproductibility of variability appears very unconstant. This study suggests that fourteen repeated measurements of BP values over a fortnight period allows a better estimation of BP level at rest. It cannot be equivalent to 24 hour BP record to estimate variability.

NEPHROTOXICITY (NTX) OF TREATMENT BY INTERLEUKINE 2 (IL2) IN CHILDREN WITH NEUROBLASTOMA

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Intravenous administration of IL2 has been proposed in the treatment of several type of metastatic cancers in adults. Three children with stage 4 neuroblastoma were included in a phase 2 trial and received 5 courses of IL2. Since renal toxicity is probably a dose-limiting side effect, a prospective study of hemodynamic, metabolic and renal disorders was carried out over a 9 days period. Maximum changes in renal parameters were seen between day 4 and day 8. Fluid retention occured with oliguria, decrease in fractional excretion of Na (FeNa) from 1.4 % to 0.3 %, associated with weight gain (+ 10 %). There was simultaneously a renal failure of pre-renal type (Cin = 86 ml/mn/1.73 m2 at day 1 and 8 ml/mn/1.73 M2 at day 6) ; the subsequent tubular lesions lead to severe cytologic abnormalities, increase of enzymuria and Na leakage (FeNa = 3.6 % at day 9). These abnormalities as well as the other side effects (fever, chills, erythema...) disappeared soon after stopping the administration of IL2.
IL 2 leads to hydrosaline inflation in the interstitial compartment and to plasmatic hypovolemia by increasing capillary permeability and decreasing systemic vascular resistances ; the role of a major release of histamine is discussed. It results in a functional renal failure with an acute tubular necrosis, leading to a transient tubulopathy with Na leakage. This NTX is probably enhanced by other risk factors (chemotherapy, radiotherapy, antibiotherapy...) Nevertheless, the carcinologic results are encouraging enough to make these disorders acceptable, and a better understanding of their mechanisms will probably allow a more adapted management and therefore a better tolerance.

NEONATAL RENAL FAILURE INDUCED BY INDOMETHACIN

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Indomethacin is used to prevent preterm labour. This study reports its effect on renal function in the fetus and newborn. From January 1983 to December 1985, 304 pregnant women (3,8 % of the patients seen in this institution were treated by Indomethacin with a daily dose of 175 mg.
A significant oligohydramnios was consistently noted but amniotic fluid production rapidly increased to normal, one or two days after the treatment was stopped. During this period, only 3 newborns (1 %) presented a transient oliguria with an elevated serum level of blood urea nitrogen and creatinine : the abnormalities were totally reversed in two to six days without residual abnormality. More recently in the first trimester of 1986, we observed 3 cases of renal impairement : in one case, the renal impairement was mild and transient. The second case had severe but reversible renal failure and the third case acute anuria leading to death at the age of three weeks. In this last case, histological examination revealed significant bilateral renal involvement : peripheral glomerular cysts and tubular alterations. These data suggest that the exceptional occurence of severe renal impairment should not preclude the use of Indomethacin as a tocolytic agent. However, regular echographic monitoring of amniotic fluid volume is recommanded. Systematic cessation of treatment at 34 or 35 weeks of gestation is preferable or at least one week before the birth.

INCREASED INTESTINAL PERMEABILITY TO (51 Cr) EDTA IS CORRELATED WITH IGA IMMUNE COMPLEX-PLASMA LEVELS IN CHILDREN WITH IgA-ASSOCIATED NEPHROPATHIES.

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Intestinal permeability was investigated in 10 normal young adults, in 11 control chindren and in 9 children presenting with either Berger disease (4 cases) or Henoch-Schönlein nephritis (5 cases), making use of (51 Cr) EDTA, 24-hour urine radioactivity was measured and results were expressed in percentage of the oral dose administered. Means and SD were 2.35 % +/- 0.77, 2.51 % +/- 0.70, and 5.10 % +/- 2.35 for normal adults, control children and patients with Iga-associated nephropathies respectively. The differences of permeability between controls and patients were statistically significant ($p < 0.01$). In addition, a significant, direct, linear correlation has been established between the percentage of (51 Cr) EDTA excreted in 24 Hour urine and IgA immune complex-plasma levels.
Our results therefore support the hypothesis that increased gut permeability could play a role in the pathogenesis of IgA-associated nephropathies.

EFFICIENCY OF POLYSULFONE MEMBRANE (PM) WITH HEMODIAFILTRATION (HDF) FOR PREVENTION OF B2 MICROGLOBULIN (B2M) ACCUMULATION IN LONG TERM HEMODIALYSED CHILDREN;

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B2M is the major protein precursor of amyloidosis long term dialysed patients, with predilection for bone deposits. Plasma B2M (RIA, Pharmacia) was analysed in 28 children (4-18 years) on HDF with PM on an average of 32 months (6-94 months). B2M plasma levels were high in dialysed children (34 ± 8.5 mg/l) without correlation for sex (boys 33 + 9.4 mg ; girls 34.6 ± 7.5 mg/l). B2M plasma levels were lower (15 ± 3.4 mg/l) in children with residual kidney function in comparaison with anuric children (34 ± 6.4 mg/l) without consideration of the underlying disease. B2M dialytic extraction coefficient was determined with different mode of purification using a given PM (polysulf F40) higher in HDF (O.31 ± 0.02) than in HD (0.13 ± 0.01) or HF (0.19 ± 0.01). This extraction was different according to the membrane used. Plasma B2M levels were followed up over a 5 years period in 5 children (median duration of dialysis 75 months) treated with HDF (3 x 3 h/week) using PM. Despite the effective B2M removal in every session, the predialytic B2M levels in plasma remain in the same range at the start of the study period (35 ± 7.5 mg/l) and 5 years later (39.6 ± 4.5 mg/l). One of this child had a bone cyst unrelated to secondary hyperparathyroïdism and another one joints pain (scapulohumeral periarthritis).

Long term use of polysulfone membrane in HDF condition, despite high B2M dialytic removal, cannot prevent neither high B2M plasma levels nor amyloïd deposits manifestation in children (B2M production or cellular shedding seems to balance dialytic removal).

RESULTS OF RENAL FINE NEEDLE ASPIRATION CYTOLOGY (FNAC) IN TRANSPLANTED CHILDREN

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FNAC of renal allografts was performed on 92 instances in 62 children and the results were correlated with clinical data and response to therapy. All patients received corticosteroids and azathioprine, cyclosporine was added in 25 cases and anti-lymphocyte globulins (ALG) in 26. The indication for performing a FNAC was always an increased plasma creatinine. 68 % of FNAC were performed during the first month following transplantation. The patterns of FNAC were subdivided into 5 categories according to cytological criteria, including the corrected increment (CI). Group I : 6 smears showed a normal cytology (CI = 0.64 ± 0.11) which was well correlated with clinical data. Group II : 20 smears showed tubular and endothelial lesions (CI = 0.67 ± 0.12). In 11 cases, the patients were receiving ALG and the results of FNAC were well correlated with clinical data in 5. In the remaining 9 cases, FNAC was well correlated with clinical data in 6 of them. Group III : 32 smears showed a CI of 1.78 ± 0.12. This group was composed of 13 cases without clinical rejection, 14 cases receiving anti-rejection therapy and 5 presenting with clinical signs of acute rejection despite a low CI. In Group IV (23 smears, CI + 4.02 ± 0.16) and Group V (11 smears, CI = 8.9 ± 0.91), in which FNAC was suggestive of acute rejection, a good clinico-pathological correlation was observed in all cases. The effect of ALG on CI was studied in 11 patients presenting with an acute rejection episode. CI was lower than 3.5 in all cases but one. However, when FNAC was performed after ALG with drawal in 3 patients, CI had significantly increased (mean 1.5 to 6.7). Renal biopsies, performed simultaneously in 15 patients, were well correlated to FNAC in 12 of them. In conclusion, elevated CI (> 3) was always correlated with acute rejection. Conversely, a low CI may be observed in patients with clinical signs of rejection, especially in those receiving ALG.

OUTCOME OF HEPATITIS B AFTER RENAL TRANSPLANTATION IN A PEDIATRIC POPULATION.

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To determine if immunosuppressive treatment has an adverse effect on hepatitis B after renal transplantation in children, we studied the hepatic outcome of 54 HbS Ag-positive transplanted children whose follow-up ranged from 1 to 14 years (mean = 8 years). 44 still have a functionning graft while 9 are back on dialysis and 1 died from extra-hepatic cause. 32 are chronic Hbe Ag carriers, whereas 13 have Hbe antibodies. 47 never presented with clinical symptoms related to hepatitis, 3 had transient symptoms, and 4 have persistent or progressive liver symmptomatology : 3 portal hypertensions (PHT) and 1 hepatic failure. Cytolysis was present in 37 % of patients at time of grafting and ultimately developed in another 32 %. 22 liver biopsies were performed in 17 patients; Among the 10 initial biopsies (before or at time of grafting), 4 showed severe lesions : 1 cirrhosis, 2 chronic active hepatitis (CAH), whereas 6 had milder alterations : 4 chronic persistent hepatitis (CPH) and 2 portal fibrosis. Conversely, in the 12 biopsies performed after a mean post-transplant follow-up of 5 1/2 years (9 months to 12 years), liver lesions were severe in 8 : 3 cirrhosis, leading to PHT (2 cases) and hepatic failure (1 case), and 5 CAH, and were moderate in only 4 (3 CPH and 1 peliosis). The majority (9 out of 12) of Hbe Ag positive patients who underwent liver biopsy had severe liver alterations : 3 cirrhosis, 6 CAH. Therapy seems to have little or no influence on the outcome of hepatitis ; in particular, the worsening of cytolysis was similar, whether Azathioprine was given at the same dosage, decreased or withdrawn. With Ciclosporine (6 cases), serum transaminases returned to normal in 1 patient, did not change in 2, and increased in 3. One of these 3 latter patients, who was grafted when he presented already with a cirrhosis, developed hepatic failure within one year, and underwent a successful liver graft. Although 50 of the 54 children have currently no clinical liver symptomatology, the rapid worsening of this latter patient decreases our optimism about the long term outcome of hepatitis B in transplanted children.

INTELLECTUAL DEVELOPMENT OF CHILDREN WITH SEVERE CHRONIC RENAL INSUFFICIENCY (CRI) IN INFANCY.

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Recent studies have identified developmental impairment in children with CRI from infancy. We studied the intellectual development of 13 children with severe CRI due to malformative uropathy or renal hypoplasia treated since birth or the 1st weeks of life. Mean creatinine clearance (Ccr) was 10.7 ml/mn/1.73 m^2 (5 to 22) at 1 month (m), 16 (5 to 26) at 1 year (Y), 16 (2 to 23) at 2 y. Gastric drip feeding was necessary during the 1st month in 3 cases and during a mean period of 29 m (5 m to 4 y 6 m) in 5 cases. Mean duration of hospitalization or of stay in a medical institution during the 1st y was 194 days (< 2 m : 2, 2 to 4 m : 4, 4 m to 1y : 7). Nine children received aluminium (Al) gels, 8 at a low dose (mean : 55 g, 27 to 90), 1 at a higher dose (585 g). Mean loss of SD for height was 1 ± 0.95 (mean ± SD) the 1st y, 0.11 ± 0.98 the 2nd y. The weight to height (W/H) ratio (normal > 90 %) was 84 ± 10 % at 1 y, 86 ± 6 % at 2 y. Eleven children came from a low socioeconomic level group, 2 from a middle level group.

Verbal (V), permormance (P) and full-scale (F) intelligence quotients (IQ) were measured by the Wechsler Preschool and Primary Scale of Intelligence and the Wechsler Intelligence Scale for Children-Revised 1981, at a mean age of 7 y 4 m (4 y 5 m to 15 y 8 m). At this time, 3 children had a functional kidney graft (performed at age 5 to 8 y), 1 was on hemodialysis, mean Ccr was 12.7 (6 to 30) in the 9 others. Mean F IQ was 89 (73 to 106), V IQ 94.7 (79 to 124), P IQ 85.6 (69 to 112). F IQ was > 100 (101 to 106) in 3 children (23 %), <100 in 10 (77 %). Among those, IQ was 87 to 92 in 6 children (46 %), 73 to 84 in 4 (31 %). IQ of the 3 transplanted children (87.7 ± 12) was similar to that of the other children (89.5 ± 10). A significant inverse correlation ($p < 0.05$) was found between IQ and duration of stay in hospital or medical institution during the 1st y. There were no significant relationships between IQ and severity of CRI, growth gain and W/H ratio during the 1st 2 y, or between IQ and Al loading.

In conclusion, severe early CRI did not induce major intellectuel impaiment. Nevertheless, 77 % of children had IQ in the low-normal range or below normal. This proportion is greater than in normal children of similar socioeconomic level groups. Reduction of hospitalizations and of separation from the family, and better nutrition, might help to improve the intellectual capaciaties of these children.

FETAL URINE COMPOSITION : CLINICAL APPLICATIONS

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Thirty one fetuses with bilateral or low urinary tract obstruction were studied systematically. Fetal urine samples were performed under ultrasound control, for the study of 14 biochemical parameters. We established the correlations between the prenatal levels of biochemical parameters and the renal function after birth. According to post-natal renal function, we defined three groups of patients : 1) those with severe renal impairment incompatible with postnatal survival. 2) the surviving ones with abnormal renal function. 3) those with normal renal function. We confirmed the poor prognosis of high levels of sodium, and elevated osmolarity of fetal urine. However, urea, creatinine, ammonium and beta 2 micro-globulin level seemed to be more accurate markers than sodium and osmolarity. But the most interesting parameter was calcium since it was the earliest marker of abnormal renal function. Calcium levels rose with the evolution of urinary tract dilatations, and we discuss the possibility of using calcium levels to follow the progress of renal failure and its recovery several months after birth. Importance in defining these three significant groups prenatally is to be able to select the candidates for shunting and to determine the efficacy of decompression of the urinary tract in these fetuses.

HARVESTING ORGANS IN CHILDREN FOR TRANSPLANTATION

(A retrospective study of 45 brain dead children)

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The remarkable progress in organ transplantation leads to a dramatic rise in the demand for organs. Pediatric intensive care units (PICU) are involved for harvesting organs, but organs are collected from a limited number of potential donors. That situation is more an organizational and voluntary problem than a technical one. We performed a retrospective study of 45 brain dead children (23 boys and 22 girls) admitted in our PICU from 1980 to 1987 in order to define failure in organ harvesting. The mean age was 7.6/12 years (1 day to 15 years). Contraindications were observed in 16 children (36 %) : infection (5 children), cardiac arrest (5), abdominal injury (3), spina-bifida (1), unexplained thrombopenia (1). Age was considered too low in 1 newborn.

A lack of organization was noted in 5 cases (11 %) because it was a legal holiday with difficulties to gather a surgical team or because the unit was too busy or the physician on duty was unmotivated. Parents refused in 7 cases (15 % of all braindead children but 25 % of brain dead children without contraindication). Organ retrieval was performed in 17 cases (38 %).

We have observed a better parents'acceptance since the interview had been conducted by a nephrologist who was implicated in a transplantation program. Progress in transplantation development requires motivated medical teams for obtaining organs. Numerous psychological barriers could be removed by providing education to nurses, physicians and families.

USE OF CYTOMEGALOVIRUS HYPERIMMUNE GLOBULIN (HIG) TO PREVENT PRIMARY CYTOMEGALOVIRUS INFECTION IN KIDNEY TRANSPLANTED CHILDREN.

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High-titred anti-CMV IgG antibodies (HIG) were used, in the frame of a randomised protocole in CMV seronegative children in order to prevent primary CMV infection. 28 children, 27 cadaveric kidney recipients and 1 living related kidney recipient, were assigned to receive either CMV HIG or no treatment. Cadaver donors anti CMV serology was unknown. The HIG was given intraveinously at a dose of 250 mg/kg just before and 15, 30 et 45 days following transplantation. Between June 86 and June 87, 13 children were treated (group A) and 15 were untreated (group B) with a minimum follow-up period of 3 months. Seroconversion was observed in 4 of 13 patients of group A (31 %). 3 Developped IgG and IgM anti-CMV antibodies, 1 developed only IgG on high titer persisting several months after the last globulin infusion. The virus was isolated in the urines of a single child. The clinical features were : prolonged fever (temperature 38° C for more than 7 days) in 3 cases, hematologic abnormalities (platelets 80000/mm3 or white cells 3000/mm3) in 4 cases, increase of serum transaminases (> twice the upper limit of normal) in 1 case. Rise of creatinine level occurred in 4 children and the acute rejection reaction was confirmed by renal biopsy in 2 of them. None of those 4 lost his graft. In the group B, seroconversion was observed in 5 of 15 patients (33 %). 5 children developed IgG anti-CMV antibodies and 2 developed IgM. 2 patients had a viruria and 1 patient had a viremia. One child was asymptomatic and among the others, 4 presented with prolonged fever, 4 with hematologic abnormalities and 3 with increased transaminases. Two grafts were lost in this group, but without clear relationship with CMV infection. The absence of difference between the 2 groups suggests that the preventive use of intravenous HIG cannot modify the incidence of the primary CMV infection in kidney transplanted children, nor the severity of the disease.

INTERSTITIAL NEPHRITIS WITH CHRONIC RENAL FAILURE AFTER INTOXICATION WITH CORTINARIUS SPECIOCISSIMUS MUSHROOMS IN A FOURTEEN YEAR OLD BOY.

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A fourteen year old boy was admitted with a history of nausea, vomiting, abdominal and flank pain and oliguria after having been treated for suspected urinary infection for two days with cotrimoxazole. When seen in hospital, the previously healthy boy was afebrile and remarkably well. He complained of pronounced bilateral loin pain. The clinical examination did not reveal any particularity. Blood pressure was 150/80, there was no evidence of hyperhydratation. His serum creatinine was 946 mol/l, sodium 131 mmol/l, potassium 6.7 mmol/l. Haemoglobin was 16.1 g/dl, leucocytes 9 x 10^9/l and platelets 245 x 10^9/l. Liver enzymes and immunological tests were normal. Diuresis ceased completely soon after admission and haemodialysis had to be started. Sonographically, the kidneys appeared slightly enlarged.

^{125}Iode-hippuran scan showed a shock kidney pattern lacking tubular clearance. Transcutanous renal biopsy was performed. It did not reveal any significant glomerular alterations, but interstitial nephritis with edema and a mixed cellular infiltration by lymphocytes, plasma cells and few eosinophilic as well as neutrophilic granulocytes. After five days of anuria diuresis started slowly. But renal function did not normalize, and the boy continued on regular intermittent haemodialysis twice a week. At a later renal biopsy progressive fibrosis was noted. Renal transplantation was carried out 15 months after poisoning. History was empty for nephrotoxic agents exept for mushroom ingestion. Up to five days before admission the boy ate several mushroom dishes, raw and cooked, which he had collected and prepared for himself. He retrospectively identified some of the mushrooms as being cortinarius speciocissimus which is occuring increasingly in the surroundings. Poisonings by mushrooms of the genus cortinarius (orellanus syndrome) are characterized by the long delay (2-17 days) between ingestion and appearence of symptoms. Renal damage varies from mild with complete recovery to severe with irreversible loss of function. Characteristically, there is no involvement of other organ systems. In interstitial nephritis of unknown etiology the possibility of mushroom poisoning should be considered.