

To help research, help us to make the Fondation Motrice known!

The Fondation Motrice has entered its third year of existence, and the urgency remains as always : to rally all means to expand Cerebral Palsy research. We regularly appeal to your generosity in order to collect the necessary funding for new projects, but you can also **play an important role by making the Fondation**

Motrice and CP known in your own circle, to your family and friends, and also in your professional, associative or institutional environment.



Through memberships we must broaden the network of those who already support us : people with CP themselves, their families, the associations which represent them, specialized establishments and the consultants, researchers, and – in order to reach the general public – private sponsors and public funds. The voice of the Fondation Motrice needs to be amplified in order to mobilize public or private financing for research. Help us to make our voice heard! **The Fondation Motrice is the only research Foundation dedicated to CP in France, and in 2007 it could only dedicate €250,000 to research, the equivalent of €2 per person affected!**

As the primary cause of physical disability in children, Brain Injury / CP affects roughly one in 400 children in Europe and the US annually. Today, in Europe, there are approximately 650,000 adults and children living with brain injury / CP. It is for them and for their families - who must cope with the daily difficulties connected with this disability in all its facets ; it is also to prevent new cases that we must multiply our efforts.

For this, we must advance the research into the prevention of cerebral lesions and their treatment, but also in the domain of re-education, physiotherapy, technical aids, pain management, and in all that contributes towards an improvement in quality of life and active participation in society.

We must make their voices heard and provide the means for researchers to bring about future progress.

Spread the word, they are counting on you !

Dr. Alain Chatelin
President

THE FONDATION MOTRICE

4 Rue du Pic de Barrette 75015 PARIS

tel : +33(0)1 45 54 03 03

secretariat@lafondationmotrice.org

www.lafondationmotrice.org

Foundation recognized as being of Public Service by decree 4 July 2006

Patron

Mr. Andréa CASIRAGHI

Founders

APETREIMC (2005)

SESEP (2005)

CDI (2005)

PASSERAILE APETREIMC (2006)

Administrative Council : Dr A. CHATELIN (President), Dr L.HERTZ-PANNIER (General Secretary), M.P.FRANCOIS (Treasurer), Dr. D.COSTANTINI, M. R. FERNANDEZ, Pr D.HOUSSIN, M. P.JACOB, Mme M.LE MOING, M. E. POSTAIRE, Pr R. RAPPAPORT, M.P.TOULLET, Pr L.VALLEE

Scientific Council : Pr M.VIDAILHET, (President), Pr A.BENABID, Dr C.BERARD, Dr C.CANS, Pr G.CIONI, Dr P.GRESSENS, Pr P.HUPPI, M. E.JACOTOT, Pr I. KRAEGELOH-MANN, M. M.LE METAYER, Pr G.PONS, Dr B.ZALC

Dossier

MEDICATION



Today, medicine still lacks clinical studies among children. Professor Gérard Pons, member of the Scientific Council of the Fondation Motrice and Vice-President of the Pediatric Committee of the European Medicines Evaluation Agency, helps us to better understand the difficulties and the issues involved in the research into medication with regard to children.

1. Why must one undertake specific studies for children rather than simply extrapolate the results obtained from adults?

There are several reasons for this :

- firstly the reaction of the medication in the organism (their absorption, their dispersion in the system, their metabolic transformation, their elimination etc.) present differences according to age ;
- Also, the impacts of the medications are different. The organs might react more, or less, in the child as in the adult. Besides, a child's system presents the particularity of being in full growth, and undesirable effects that one doesn't see in the adult, may become apparent in the child through a disturbance in their growth and development ;
- Finally, one must not forget that certain illnesses exist in the child that do not exist in the adult.

2. Why have there been so few studies carried out on children up to the present?

The main reason is that of profitability for the laboratories. The illnesses must be frequent and represent a market large enough for them to recoup their investment. The direct consequence of this is that certain medicines are prescribed to children which have not received market authorization (MA)* due to the lack of a study, hence the practitioner can not be fully aware of the effects which the substances may have on their patients.

The second reason concerns the difficulty in "recruiting" children for the tests : it is necessary to have the agreement of both parents, and the assent of the child as soon as they are old enough to express themselves, thus rendering this preliminary stage in the study longer, and therefore more costly. Parents are not sufficiently informed about clinical trials which make them fearful and hesitant. They do not realize that a prescription outside of the framework of the AMM presents a greater risk to the child than the participation in a clinical trial.

Lastly, we must not negate the fact that there is a lot of reluctance towards taking risks with children, as the laboratories may be sued in case of a problem.

3. What difficulties are faced when undertaking a study?

One might think that the first difficulty would be one of ethical concerns : however it must be acknowledged that the prescription of medications outside the confines of the MA which is currently practiced by doctors, is far less ethical than a clinical trial. It amounts in effect to an “uncontrolled” test, without a framework, without proper risk calculation and without shared knowledge. In reality, parents would do better to authorize the participation of their sick children in clinical trials if an effective and sufficiently safe treatment doesn’t already exist. This is even truer when the illness is severe and can endanger quality of life or life itself.

The principal difficulty is therefore is the recruitment of children for the trials : the general public does not realize that many prescriptions outside of the AMM framework are prescribed daily. In the case of families with children who have rare, grave or chronic illnesses, the information is better and the parents are less reluctant to participate in studies ; they even ask for them. But most parents hesitate at the idea of transforming their children into guinea-pigs, even though the tests are very well supervised and strict methodological tools have been put into place to protect the children from negative effects of the medicines.

There remains, finally a “technical” and ethical difficulty, the invasive aspect : sample taking can be painful and their repetition can cause problems.

4. What are the solutions therefore?

The first is to better inform the parents and public opinion, the second is to develop innovative methods which limit the invasiveness and sample taking.

Today we also have another powerful tool : the Ruling on pediatric medicines put forward by the European Union and effective since January 2007. From now on, each request to the AMM must be accompanied by a proposal of clinical trials with children : the industrialist must submit a Plan of Pediatric Investigation in accordance with the Pediatric Commission of the European Agency of Medication. If the content of the Plan is respected, the industrialist will obtain 6 months of protection for the findings which is an attractive financial advantage for the laboratory.

The role of the European Medicines Evaluation Agency (EMA)

The EMA is responsible on behalf of the European Union regarding questions relative to the evaluation of quality, security and effectiveness of medical products for human or veterinary use :

- It co-ordinates existing scientific resources and those placed at its disposal by member states.
- It furnishes the best scientific advice possible to member States and European institutions

*The MA is the Market Authorization agency.

How can we minimise the risks of brain injury that occur at the moment of intensive care of the newborn? We ask Véronique Zupan-Simunek, pediatrician, practitioner in neonatal intensive care at the Antoine Bécclère Hospital in Clamart.

1. In what cases do infants need intensive care at birth?

There are two main situations. 80 to 90% of these represent cases of prematurity or extreme prematurity where the new-borns need respiratory or nutritional assistance. The other situation constitutes cases of vital distress in the hours immediately after birth, for example due to a lack of oxygen during the birth or because of a serious infection which affects the new-born. In all cases, the urgency is to preserve the vital functions, and primarily to ensure respiratory assistance to the infant. Once this urgent situation is under control, the infant is cared for globally with constant concern for maximising protection of the extremely vulnerable brain.

2. What resources do you have for protecting the brain of the new-born?

Unfortunately there is no suitable medication which prevents Cerebral Palsy. On the contrary, we are always afraid to use substances to care for a child which could be toxic for the brain, like steroids, generally beneficial for brain maturation, but some have been found to be dangerous. However, these days we do possess techniques and the result of studies which help us. In the case of prematurity, we know that the brain is extremely fragile and at risk of haemorrhage : specialized units have therefore learned how to handle the child whilst taking infinite precautions to avoid any sufferance or destabilization. Certain medications can also help, such as morphine, but the crux lies in the expertise of the care-giving teams. For infants born at full term but who have suffered asphyxia at birth, studies published in 2005 have shown us that controlled hypothermia can help to protect the brain.

3. Are there any new drug treatments on the horizon?

We first need long-term safety studies which would assure us that the medications that we need to care for an infant do not present any risk to the brain during this period of extreme vulnerability. In addition, we know that nutritional factors play a role in causing brain injury : at birth, the premature baby is cut off from substances – notably hormonal – which come from the mother and which contribute to the development and maturation of the brain. When we are able to identify these substances, we will be able to provide them to the child, as, today we can nourish them on glucides, lipids and proteins.



3 Questions for Etienne Jacotot, member of the Scientific Council of the Fondation Motrice and founder in 2001 of Thérapstosis, a bio-pharmaceutical company originating from a research laboratory of the Pasteur Institute.

1. Your company, Thérapstosis, works on the prevention of cerebral palsy. Could you describe the object of your research and explain to us how medications can react at the moment when the brain is threatened?

The situations at the root of cerebral lesions in the new-born are acute situations which require rapid intervention. Two families of medicines can improve the prognosis for newborn infants after brain injury : cytoprotectors and regenerative agents. Furthermore, these two types of medicines can act in a complementary manner :

- the role of cytoprotectors is to prevent or block the process of cellular death
- regenerative agents not only reduce the phenomena of cellular death, they also encourage the substitution of damaged cells or stimulate the connections between neurons.

We already know of a certain number of substances likely to act on the process of cellular death, but, for many of these medicines, the difficulty is access to the brain in getting past the hemato-encephalic* barrier, even though it is less hermetic in the newborn infant than in the adult. Today, it is difficult to predict what medicines will be effective tomorrow. Our research is dedicated to developing the inhibitors of cellular death in the newborn brain.

2. The Fondation Motrice has awarded a grant to a researcher, Mme Le Tourner, who works on one of the products from your laboratory. What will the grant be used for?

The aim of this project is to evaluate the correlation between the reduction of the size of cerebral lesions and the improvement in behaviour in newborn rats treated with a new neuroprotector, the TRP601, after having suffered an oxygenation defect of the brain.

3. Do you consider that there are a sufficient number of projects of this nature being undertaken in the industry?

No, in effect, there should be many more projects and notably the development of a standardized animal blueprint.

It essentially boils down to a question of financial means and a mobilisation of competencies. This is why tripartite collaborations between private research, public research, and organisations like the Fondation Motrice, that support research, must grow : they allow for different viewpoints and exchanges of knowledge and know-how, and this “fertilization” is essential if new medicines are to see the light of day.

*

The role of the hemato-encephalic barrier is to filter the passage of substances from the blood to the cephalo-rachidien liquid in order to preserve the central nervous system.

Under the microscope **botulinum toxin**

Botulinum toxin has been used for over 15 years in the treatment of certain inappropriate muscular contractions associated with Brain Injury / Cerebral Palsy



A physiotherapist's point of view : Philippe Toullet, Rehabilitation Director of the Training Institute of Cerebral Motivity.

1. How is botulinum toxin used?

Botulinum toxin was used in the mid '80's to treat adults suffering from neurological illnesses that caused irrepressible and uncontrollable muscular contractions such as involuntary blinking or spasmodic torticollis. Botulinum toxin is injected at the junction between the nerve and the muscular fibres. It blocks the nerve impulses by suppressing the production of acetylcholine and prevents muscular contraction. The magnitude and duration of the paralysis of the muscle depends partly on the amount of toxin that is injected and also on the precision of the injection. Injections of botulinum toxin for children began in France in the early '90's, first in the triceps to treat equinism of the foot (the difficulty of placing down the heel when walking), then progressively in other muscular groups of lower and upper limbs.

2. What are its actual benefits?

For people with CP or multiple disabilities, botulinum toxin is a valuable tool in orthopedic prevention, functional improvement and also for providing comfort and relaxation. Its effect, however, is localized and of limited duration. It is used as an occasional help to overcome a difficulty that rehabilitation or remedies cannot solve. It allows a « therapeutic window » to open, during which time the child, being free of inconvenient contractions, will be able to learn a new motricity.

3. Is botulinum toxin a remedy for all problems linked with contractions ?

Unfortunately no, its scope is limited as it acts on pathological contractions (contractions at rest, those associated with effort, with speed, etc.) but not on the lengthening of shortened muscles. This type of contraction is sometimes a way to compensate for a problem located in another area and is part of a global equilibrium between the muscles controlled by the brain. Therefore, it can be used only after an accurate evaluation of the « stiffness » to be treated.

4. Are there side effects ?

They are rare. There is occasionally some pain in the spot which was injected, and some general but temporary fatigue. As a rule, Injections must be made at the very least two months apart. In some children the expected result is not achieved, either because the targeted deep muscle has not been reached - its location may not have been possible to find with the ultrasound scan, or the presence of antibodies prevented the toxin from producing its effects. This last reason explains why the injections are not repeated too often as their effects tend to diminish if they are too frequent. The EMEA (European Medicines Evaluation Agency) has reported very rare undesirable side effects related to the remote diffusion of the product. That is why injections of botulinum toxin must be administered by experienced doctors.

First-hand account -

From an interview with Meïr, aged 20.

« I had toxin injections when I was younger to avoid operating on my legs. The treatment was not sufficiently efficient and I had to undergo the operation anyway, but thanks to the toxin the operation was done later than it would have been otherwise. I was a kid, I was scared of the pain even though I was told that I would feel nothing more than a mosquito bite ... it was true, but after 5 or 6 injections, I was in pain ! Some years ago, all the treatments against pain did not exist. After the injection, it was very strange to feel the liquid going through my leg and I had to be very careful not to lose my balance. But it was also a good thing because the toxin relaxed my muscles and that helped me during physiotherapy. I would say that toxin injections are only truly efficient when combined with intensive physiotherapy, i.e. working almost every day with a physiotherapist. The problem is putting up with that. When you are a young kid, you don't understand why you have to do the physiotherapy instead of playing with your friends and now that I am an adult, it would be difficult for me to find the time to do it while studying. »

Your donations are vital for research to progress !

IMC/PC still affects 1 child out of 450

By making a donation to Fondation Motrice, you get important tax discounts
(*applicable regulations as of 15.3.2008*)

* **Individual donors** can choose between two discounts :

- if you pay income tax, every 100 € donated to research will cost you only 34 €. You get a discount of 66 % on the amount donated, up to a maximum 20 % of your taxable return (art. 200, Tax Code)
- if you are subject to wealth tax, every 100 € donated will cost you only 25 €. You get a reduction of 75 % of the amount donated, up to a maximum of 50 000 € (art. 885-0 V bis A, Tax Code).

Fondation Motrice News

The first general assembly of the **Association of Friends of the Fondation** (AFOM) was held last January 18th.

The **Administrative Council** from now on is composed of 10 members : 8 elected representatives of the active members and founders (P.Carnot, D. Chastenet de Géry, E.Coutelle, F.Flaschner, J.Helfer, P.Jacob, S.de Larminat, P.Motte, M.Perin, F.Tedeschi) and 2 ex officio members (M.Baron, President of the French Federation of Brain Injury Associations (FFAIMC) and A.Chatelin, President of the Fondation). A new organization has also been set up between the Fondation Motrice and the AFOM to allow for shared presidency and administration.

On February 12th, the Administrative Council (AC) elected its board :

President : Alain Chatelin

Vice-President and representative of the AFOM at the AC of the Fondation Motrice :

Pascal Jacob

Treasurer : Pierre-Elie Carnot

General Secretary : Marie Perin

On April 17th, the AC co-opted Valérie de Brem.

Prospective Study : progress report

The Fondation Motrice has launched a prospective study, supported by the CNSA (National Trust of the Solidarity for Humanity), with GERPA (P.Chapuy, R.Monti) et D.Ejnes, project manager, to assess expectations and needs in terms of research into Brain Injuries/ CP, as well as the feasibility and timeframe for significant progress. The results will notably help to identify and prioritize the most important fields of research for future awarding of grants. In its preparatory stage, the study will consist of collective brain-storming workshops - with all concerned parties - which will take place on the following dates :

1. March 26 2008, group of people with brain injury and their families – the objective is to vocalize the expectations and needs of disabled people, and their priorities.
2. April 16 2008, group of researchers, doctors and therapists – the objective is to determine the most important and promising fields of research.
3. April 22 2008, group of interdisciplinary professionals – its objective is also to determine the research fields of utmost importance.

Our Benefactors and Supporters

3 Questions for

.... **Jacky Vagnoni, President of the ADIMC of Haute-Savoie.** Created in 1965 by a group of parents, ADMIC 74's mission is to assist people with brain injury, multiple disabilities, and, more broadly, people with motor function disabilities -with or without associated problems - during their lifetime, to represent them, and to run establishments for children, adolescents and adults.

1. You have circulated the previous Foundation's newsletter among the members of your association, what reaction have you received? What are the expectations of the people you represent, as regards research into Brain Injury / CP?

We distributed the letter to all of our members, as well as our partners (administrations, elected representatives, sponsors). The members of the association were both amazed and very happy to learn that the research is specifically related to brain injury. Now, they would like to be kept informed.

Concerning the research, the expectations are very diverse and include prevention, care, rehabilitation techniques, technical developments and innovation towards social integration. With regards to this last point it is clear that brain injury is still "unseen" by the general public, and this lack of recognition works against people with brain injury. We are therefore awaiting action on the part of the Fondation Motrice that will help shed light on their needs and thus contribute to making brain injury more easily understood.

2. One of your executives, François Revol, participates in a Pilot Committee of prospective study launched by the Fondation Motrice. What motivates this involvement on the part of your association?

It is a response to a real need that a grassroots organisation participate in order to "validate the methods of the study, to be a source of useful contacts for identifying people, for interviews and workshops, and to contribute in evaluating the relevance of intermediary results in order to better focus the study if necessary". For the ADIMC of Haute-Savoie, this involvement is part of our plan of action which is, principally, to encourage research and the training of professionals.

With regard to François Revol, I know her interest in research. Furthermore, her twin responsibilities as both an administrator and a care-giver, is an enlightening and relevant addition to this pilot group.

3. In your opinion, what is the message that should be addressed to the general public in order to support brain injury research?

The main message is the large number of people living with brain injury in France, the difficulties that they encounter daily on a material level, on a physical level (dealing with pain), and on a psychological and social level, and the need for mobilization to help them face these difficulties and improve their quality of life. On this subject, I think it's very important that the research takes their needs and expectations as a starting point. For the general public, getting to know people with brain injuries on a personal basis, is a chance to dispel their apprehensions and change their perceptions. This is a task for the Fondation Motrice, because the limited financial engagement of public funding means that solidarity must be found through other means such as voluntary work and Research Foundations.

EVENT

Dinner sponsored by the perfume industry : € 90,000 raised in aid of research

Daniel Chastenet de Géry (pictured here), father of a young girl who has a brain injury, and a member of the Friends of the Fondation Motrice, mobilized the perfume industry sector for the benefit of Brain Injury / CP research during a dinner organized on April 8th at Maxim's, under the patronage of Andrea Casiraghi. Participants included BPI, By Terry, Chanel, Clinique, Coty Prestige, Dior, Estée Lauder, Firmenich, Givenchy, Givaudan Quest, Guerlain, Hermès, Interparfums, Kenzo, L'Oréal Luxe, Puig, Shiseido, Takasago, Thierry Mugler Parfums and Yves Saint Laurent Beauté. Matthieu, a disabled friend of Andrea Casiraghi, gave a very moving speech.

Also present were the Princess of Kuwait, Fajer Al Rajan, Pierre Cardin, Helena d'Arundel, Elie Barnavi, Violaine Claudel, Professor Tardieu and Dr. Quentin among numerous other friends of the Fondation Motrice who wanted to show their support for Brain Injury research.

Many thanks to Roberto d'Olbia, Michel Fages and Patty Canac, and also to Christofle, Cartier, Roederer, Hermès, Lalique, Baccarat, Hédiard, J-P Gaultier, N.Rodriguez, Lacoste, Dypique and Hennessy who contributed to the evening as well as Matthieu Chatelin, Sébastien Talon, Elsa Lévy-Cado and Marie-Sophie Bahler for the organization.

A video for the Fondation Motrice

A video clip was made during an internship by a group of young friends of the Fondation Motrice, and directed by Florimond de Beler. It is an invitation to change one's regard towards disability and to unite in order to advance research.watch it on

www.lafondationmotrice.org

Thank you

.....to all of the clinics (Lille, Lyon, Paris, Saint Maurice) and associations throughout France who circulated our previous newsletter : ADIMC (from Côtes d'Armor, Haute Savoie, Ile et Vilaine and ADIMC de la Sarthe) also APETREIMC, ARIMC Béarn, ARIMC Rhône Alpes, ARIMOC Pau Béarn, CDI, FFAIMC, GIMC, Institut Le Mai, Institut Notre Dame, Passe r'aile APETREIMC, SESEP.

Please feel free to do the same in your community, wherever you may be !

Please circulate our newsletter available at <http://www.lafondationmotrice.org>



4 rue du Pic de Barrette
75015 PARIS
tel : +33(0)1 45 54 03 03
www.lafondationmotrice.org
secretariat@lafondationmotrice.org

Yes, I support La Fondation Motrice *bulletin of support*

Surname : First name :
Address :
Postal Code : City :
Country :
Tel : Email :

I wish to donate the sum of :

☐ € 40 ☐ € 60 ☐ € 100 ☐ € 150 other : €
by cheque payable to “La Fondation Motrice”

If you wish to make your donation by monthly standing order, please contact us.

La Fondation Motrice is recognised as a public service : your donation gives you the right to an important tax reduction depending on the amount of your donation .

With this donation you will automatically become a member of the Friends of the Association, unless you wish otherwise.