

Duchenne Muscular Dystrophy

What can we do for our sick children and what should we not do?

An Interview with Professor Rudolf Korinthenberg.

Professor Rudolf Korinthenberg is medical director of the Department for Child Neurology and chief of the muscle clinic at the Center for Pediatrics and Youth Medicine at the University of Freiburg in Germany. On 15 February 2006, Dr. Guenter Scheuerbrandt spoke to Professor Korinthenberg about the possibilities which are now available to the parents and the doctors for treating and managing a Duchenne boy as long as there is still no effective cure for the disease. The following text is a shortened version of the recorded interview which has been approved by Professor Korinthenberg for the information of the Duchenne families and their care givers. The questions of Dr. Scheuerbrandt are printed in italics.

Clinical trials with prednisone and cyclosporin.

We should begin with a discussion about the clinical trial with prednisone and cyclosporin which you are directing in Germany.

Duchenne muscular dystrophy is, unfortunately, still a disease which, because of its genetic causes, is not curable. Therefore, in addition to research for an effective cure, we have to look already now for treatment possibilities which could at least alleviate the course of the disease. At the moment, the two cortisone preparations prednisone and deflazacort are the only drugs known which bring a noticeable improvement for the children and their families.

But the prednisone treatment has side effects, which have been known for a long time and which are also present in Duchenne boys. We and some colleagues have, therefore, thought about how we could reduce the prednisone dosage, e.g., by giving the normal dosage, however not continuously but only 10 days in a row and then interrupting the treatment for 10 days so that one still gets the effect this way but avoids the side effects.

We have tried this but then have seen that the effect is somewhat smaller than when prednisone is given continuously daily. In order to improve this situation, we had the idea to combine it with cyclosporin. Cyclosporin is a drug which reduces the immune reactions. It has a different mechanism of action than cortisone. It also has side effects, but during a long-term treatment, they are somewhat more favourable than those of prednisone.

Our study with this combination started at the beginning of 2004. At the moment, we have 120 patients who are being treated or who already have completed their treatment. Each patient participates in the study for 15 months. In order to evaluate the study correctly, we need 150 patients, i.e., we still need 30 more whom we hope to recruit in 2006 and whose treatment will last till 2007, so that we will be able to analyse the study at the beginning of 2008.

Any results about the effect of cyclosporin are not available yet, because we are doing a double-blind study, i.e., neither the patients nor we, the scientists, know whether a particular child has received cyclosporin or a placebo, a neutral substance, in addition to prednisone. But we can say that the study is functioning very well and that no severe side effects have appeared. Of the 120 patients, only two had to leave the study, one, because he lost his ambulation relatively soon, and the other, because a diabetes manifested itself which we had not discovered

before his enrolment.

Prednisone.

For the treatment with prednisone alone, professor Victor Dubowitz prefers to give the normal dosage of 0.75 mg/kg/day for 10 days and then to interrupt the treatment for the next 10 days. This means that the children are getting, on average, only half of the normal amount. Should one do it this way or rather give prednisone, as before, every day without interruption?

This question is difficult to answer, because there are no really reliable data. We have, together with Professor Reitter in Mainz participated in the first German study with prednisone and deflazacort and given daily the normal dosage. At that time, we were satisfied with the long-term effect but we also have seen the side effects.

Therefore, I decided already a few years ago to try the Dubowitz scheme and to give the intermittent dosage schedule. I have always discussed this with the parents quite openly, and then we have decided together how we should proceed. Our experience with the intermittent dosage was that the side effects are really reduced. But there exist no real good studies about this. It seems, however, that the therapeutic effect is also somewhat reduced, and that was the motivation for adding cyclosporin.

For one year now, a large European study is being prepared which will be directed by Professor Kate Bushby in Newcastle and which should answer the questions: What is better, prednisone or deflazacort, and what is better, the daily treatment or some form of intermittent treatment in order to reduce the side effects? I am planning to participate in this European study with our patients as soon as our study has been concluded.

In my consulting hours, I explain to the parents the pros and cons of the prednisone treatment in all details, because we have still parents who do not want this treatment. They say, if it does not cure the disease, then we do not wish to risk the side effects. This is acceptable. But most of the parents are for the treatment. Then I discuss with them whether we should give the real effective dosage with the side effects or whether we should apply the intermittent therapy which certainly has fewer side effects. But there is also a third way, that one starts with the high dosage and, when side effects appear, that one changes over to the intermittent treatment. As the situation is at the moment, one can only discuss this individually with the families.

Proven data about which is better, do not exist yet.

Creatine.

Let us talk now about creatine which many parents give their children because they think it would help and does not have any side effects. Sometimes, it is even said that creatine could replace prednisone entirely or to a certain extent.

Creatine has been discussed for 10 years or more. The statement that creatine would be so effective that it could replace prednisone, that is has the same effect but without side effects, that just cannot be correct. We cannot see this in any data. Several studies were done with creatine for muscle diseases, some of which showed a slight effect. Such studies with adolescents and adults have, e.g., shown that during the duration of a study of about six months, the muscle force, especially of the arms, had increased by about 5 to 15% of the force at the beginning. Similar experiences come from sports medicine where a force increase of a similar order of magnitude was obtained by medium-distance runners and weight-lifters.

In July 2005, the CINRG (Cooperative International Neuromuscular Research Group) under the direction of professor Diana Escolar in Washington published the results of a double-blind study with creatine and also with glutamine, which showed some positive effects that, however, were not so pronounced as to be statistically significant. I.e., the observed differences were so small that it could just have been an accident that the treated children had reacted better than those who were not treated. So, this study is not conclusive. With a study in Belgium and France, where 12 boys were treated with creatine in several muscle centers, a slight positive effect on the muscle force was found.

Thus, if one looks at the data critically: creatine, or, more correctly, creatine monohydrate, seems to have a certain effect at least for the duration of the studies of mostly about three to six months. But nothing is known about the long-term effect for one or two years. There is possibly an improvement of the energy metabolism which may cause the reported effect on the muscle force or on the muscle endurance. But, according to the present data, creatine has no effect on the course of the disease. I.e., the specific symptoms of muscular dystrophy, the muscle wasting, is not being slowed down by this treatment. That is different with prednisone where we expect that there is a definite slowing of the muscular dystrophy and of the long-term loss of muscle force.

Coenzyme Q10.

There was an open, i.e., not double-blind, CINRG study with coenzyme Q10 in addition to prednisone which started in 2001 and which has now been completed. Only 15 patients were treated. Dr. Diana Escolar has told me the preliminary results: An increase of the muscle force of about 6% was found during the study period of 6 months. Dr. Escolar concludes that coenzyme Q10 in combination with prednisone could play a role, but she said also that a larger double-blind study should be performed for a final evaluation and that a dosage that is too high could cause severe headaches.

The data for vitamin Q, as we are calling coenzyme Q10 here, is still considerably thinner than for creatine. And if one looks at the literature, it is difficult to find usable data. Therefore, the results of the CINRG study are really important, although they are not yet final. It is the first study with vitamin Q performed with Duchenne patients.

Vitamin Q, also called ubiquinone, is one of the many vitamins which our body needs. It has two functions. One is that it is important for the respiratory chain in the mitochondria, the power stations of the cell. Therefore, it is clear that a vitamin Q deficiency can cause neurological symptoms, above all an ataxia. But only when there is a deficiency, and not when there is a normal supply of vitamins. The other function is an oxidation protection, similar as vitamin E. Also vitamin E has been recommended earlier for the treatment of muscular dystrophies.

Vitamin Q could possibly be helpful in muscular dystrophies, because a shortage of dystrophin can cause a chain of chemical reactions in the muscle cells which together could finally lead to muscle wasting, although one does not know precisely which of the individual steps in the metabolism is the important one. Perhaps there are pathological oxidation reactions or overloading of the mitochondria with calcium, which possibly could be slowed down by vitamin E or vitamin Q. But this has not been proven clinically for the muscular dystrophies. There exist more serious data of vitamin Q for Parkinson disease, where several studies have shown that the degeneration processes in the brain can be somewhat reduced but not prevented.

In another neurological disease, Friedreich's ataxia, the heart function can probably be strengthened by vitamin Q. These patients have a cardiomyopathy as in Duchenne patients, but for completely different reasons. This heart disorder begins very early. We ourselves have five children with Friedreich's ataxia, of whom four, at an age of seven to nine years, have already a visible heart involvement. We have first data that these heart changes can be slowed down, however not prevented, by vitamin Q. In this context, the company Santhera in Switzerland is performing a clinical study with Duchenne boys in Europe in which we participate also. We will see whether the muscle force of these patients will also become better.

It seems that there are limited effects with creatine and also with vitamin Q, but the scientific data for both compounds are not yet convincing. As they are natural substances, no side effects should be expected with normal dosages, so that a family can say: Why shouldn't we try it, because we have no other hope for an effective help? But these substances are not really cheap. Especially vitamin Q is relatively expensive. Because no convincing studies exist, these compounds are normally not being paid by the health insurances. That means, there are costs which the families have to bear. And therefore, one should reconsider, whether this money should not be better invested differently, also in the interest of the children.

Green tea. Open clinical trials.

In a new publication, professor Urs Rüegg in Geneva shows that in mdx mice, their muscle function can be improved by up to 50% if they get green tea extract. This extract is available in Japan as tablets, e.g., for cancer prevention. One should perform clinical studies with

patients, but because the green tea is easy to get, one could not prevent that the children, when they get a placebo, would also get at home green tea or green tea extract, and that therefore, one could not evaluate the study correctly. It was proposed to perform an open study instead and then simply check whether with green tea the children are better off or not. What do you think about this proposal?

Open studies are quite problematic. We have to be aware that everything we are talking about here, green tea extract, vitamin Q, creatine monohydrate, even if they have an effect at all, it would undoubtedly be only small, somewhere between 5 to 10%. This is a percentage which we often can also observe in treatments with placebo.

These substances are being tried by most of the Duchenne boys just after the diagnosis was made, i.e. when they are still quite young. A 3- or 4-year old boy with Duchenne will improve his motor activity even without any therapy. Obviously, it is not the making of the diagnosis that leads to the degradation of the muscles, but the disease has its own course. The loss of force and function generally is being noticed by the families not earlier than at the age of six to seven years. Before that time, the children continue to develop.

In an open study without giving a placebo, one does never know whether that which has perhaps improved is caused by the normal course of the disease, namely that the child is learning new things, or caused by the medication. One really needs the placebo. If one would do this with older boys who, let's say, are eight or nine years old, then the force is already so reduced, that one could really not expect anything functional from an increase of force due to creatine of only 5 to 15%, because about 10% of a small force obviously is also only a small increase.

Another practical problem is that many Duchenne boys are worse off in the winter than in the summer, because during the winter they sit inside and cannot get out, but in the summer, they play outside with their friends and are training their muscles. This observation has been confirmed by many parents. Therefore, if I am starting a study in spring, I will always get positive effects.

Thus, it would be better, one would perform a double-blind study with green tea as it is necessary for all other substances in order to prove whether the positive effects, which one believes to have seen in a few individual cases, can be repeated and therefore are really there. In order to prevent the children from drinking green tea during the study, one should have an agreement with the parents that this does not happen.

Larger clinical studies.

Many other studies with many other substances are being performed, with albuterol, oxandrolone, L-arginine etc. But what one has found in mice or with a few children, that is mostly not really significant. And then, at the end of the publication, it is always said that larger studies are necessary.

I think I should explain here what this statement means, that larger studies would be necessary. This has something to do with the methods of such studies, and this is also the reason why we need 150 children for our trial and not only 20. Natural processes mostly have a large variability.

Therefore, not every Duchenne disease is the same, and not every Duchenne boy has the same force at the same age. And other things may happen: Everyone can break his leg, it can be spring or winter which influences the muscle force, the boy can feel himself psychologically fit, can use his force well, and he can be depressed and sad and therefore cannot "give" much.

If the variability of a disease is very large, then it is difficult to prove positive changes which are not much larger than the natural variability. But in spite of this, one can prove such changes if one works with very many patients. The smaller the effect is, e.g., the increase of force which is expected from a therapy, the larger must be the number of patients, because the difference to the variability is so small.

When a small study shows that there is a small gain, as e.g. with creatine, but it is not statistically significant, then one can perhaps make the result statistically significant with two or three times as many patients, and one could also prove this small effect this way. But the effect will not become larger! It will only be more evident that this small effect is real and not the product of pure chance.

In most cases, we are dealing with substances whose effect, if it exists at all, is only small, and does not change the fate of the children and does not improve their function and their ambulation.

And even with prednisone and with deflazacort, if one evaluates all the available clinical data critically – and professor Mansur has done this in the large Cochrane Study –, one gets only a prolongation of ambulation of about two years. We have to accept the fact that all the other substances, even if they have an effect, will not be able to maintain the ambulation for a longer time.

Combined therapies.

Is it worth while to combine the different substances about which we are speaking here and which have only small effects, in order to obtain a larger activity?

Yes, because all these substances, like prednisone, creatine monohydrate, vitamin Q, etc., interfere probably with different steps of the biological processes. And, obviously, it can be that their combination results in a larger effect. But it will be almost impossible to investigate this in a scientific study, because one will always need again 150 patients for every combination of drugs. But if an effect has been proven for the individual substances, a combination should certainly be possible.

Also in our study, some patients take creatine or vitamin Q in addition to prednisone and cyclosporin. We have not forbidden the families from doing this. In order to keep the effects apart, we tell them that these additional therapies, which usually were started before, may not be changed during the study. Thus, nothing can be started and also nothing can be terminated. We have nothing against such a combination, as long as we can determine what really is being done.

Diagnostics.

We should now talk about the diagnostic measures. There is the new MLPA method of Dr. Jan Schouten in Amsterdam, which finds the deletions and duplications in the dystrophin gene. One advantage compared with other

methods is that also the deletions and duplications on one of the two X chromosomes of women can be found, so that carriers can be diagnosed even in families where the mutation of the sick child is not known. This method is used routinely for Duchenne gene analyses in the genetic laboratories in Würzburg and elsewhere. (MLPA: Multiplex ligation-dependent probe amplification.)

The problem is the point mutations which, in most cases, cannot be found with this method. But they can be found with the DGGE method in Groningen in Holland by Dr. Annemarie van der Hout for 650 euros. (DGGE: Denaturing gradient gel electrophoresis.)

If one has an unequivocal genetic test result, if one knows that a certain mutation shifts the reading frame or not, then one can predict whether the disease of the boy is a Duchenne or Becker dystrophy. Is a biopsy then still necessary?

The development of the genetic diagnoses within the last years is, without doubt, one of the very important improvements in our care for the Duchenne families. In the meantime, we have even more genetic possibilities. We cannot only determine the deletions relatively easily but also, however with more difficulties and expenses, the point mutations. We and also our colleagues in the United States, are of the opinion that the finding of a mutation that disrupts the reading frame is sufficient to prove the diagnosis of a Duchenne muscular dystrophy. And this is true also for scientific investigations which really need reliable diagnoses.

This reading frame theory is valid for about 95% of the cases, i.e., if we have a genetic diagnosis with a shift of the reading frame, then we have with 95% certainty a Duchenne and not a Becker dystrophy. If in addition, the clinical signs also agree, i.e., that the symptoms start with three or four years of age, then we are so certain about the diagnosis that we do not need a biopsy any more.

We also rely on the Dutch DGGE method. To start the analysis, we have a deletion screening performed in our department of human genetics or in Würzburg. If no deletion is found, we ask the health insurance of the patient whether we are allowed to have the point mutations looked for in Holland for 650 euros. If the insurance agrees, we send the blood to Groningen. If they do not agree, then we need the biopsy after all for a correct diagnosis.

Miracle healers and similar things.

Let us discuss now what the families should not do. They should certainly not go to Kiev to having the child examined for 45,000 euros and then to pay every half year 30,000 euros for a treatment that is not at all proved. There are some families who are interested in magnetic field therapies. This is nonsense, too, because there is no iron in the Duchenne gene and thus it will not react with any magnetic field lines. There are other nonsensical things which should be avoided.

That is correct, I agree with you here. But it is a complex subject. One should look very, very critically into all reports, into all therapy offers, which claim they could cure the disease or manipulate its course. This is true for all methods, also for the conventional medical ones. Since 1985 we know very well what Duchenne muscular

dystrophy is. Since that time, we have intensive, high-ranking Duchenne research about gene therapy, exon skipping, the many substances about which we have spoken. These research results are being extensively exchanged between the experts in countries with substantial research efforts like the United States, the UK, France, Holland, Germany, Italy, and Japan and discussed on international congresses. We know what our colleagues are doing, partly also through your research reports. And for all people who really understand what is going on, who are internationally recognized and are able to withstand public discussions, for all of them it is clear that a cure or an almost-cure of this muscular dystrophy is not possible, unfortunately. If someone claims that he knows better, then it is his duty to prove that. These proofs have never been given.

If a researcher in Kiev or Peking, or somewhere else in the world, really had serious data which were so well-founded that they are reliable, then he would continuously be present on international congresses and defend his priority so that he also would get patent protection. But this has not happened. In addition, if the results were so good as they are claimed, this would spread like wildfire among the families and many more patients would be treated than really are.

We get into another area when we have to deal with magnetic field therapies or homeopathy, even with very old homeopathic methods which become revived now. If the advocates of these methods claim they would understand more about the pathology, the pathophysiology, and the scientific facts of the muscular dystrophies, then this means only that, in reality, they do not understand at all how complex these things are.

But we see again and again that the families, not only with children who have a neurological disease, but also who have cancer or one of the many other severe diseases, that these families hope, the homeopathic therapy, the magnetic field therapy, and many other "therapies" could stabilize somewhat the general state of health of their children, support a little their resistance against infections, and improve their life quality. But the parents should not forget that there will not be a real influence on the muscular dystrophy itself.

But even these alleged positive effects have not been proven. On the other hand, we also cannot prove that they do not exist. And therefore, we do not object, when the families take advantage of such homeopathic or natural health therapies in addition to our conventional medical treatments. The psychological state is stabilized if one believes that one does at least something. Generally this does not have any side effects. But one should make sure that the child is not stressed too much. Thus, I would reject, e.g., self-blood therapies, repeated enemas, and similar measures, because they are harmful to the child, or at least they cause stress and pain and it has not been shown that they help at all. And then, one should not forget that nothing can be had for nothing, and that one is not cheated out of large amounts of money.

No therapeutic nihilism.

We have spoken much about slight effects, about perhaps-effects, and about what is allowed because it does not harm. But what should one really do?

I think, one thing should be clear, and that is my message which I give to our students and, in training courses, to our doctors: We do not live any more in a time in which one was allowed to preach a therapeutic nihilism for the treatment of the muscular dystrophies, especially of the Duchenne muscular dystrophy. It is not true that we cannot do anything. It is true that we cannot cure the disease. But we are convinced that we can help the children with the appropriate methods.

But what can we do? We can counsel the families. We can reduce the anxiety of the families. We can accompany them and be with them. We can help them to get along with the social-legal difficulties by letting them talk to our social workers and by showing them how they can manage their life with a handicapped child better, than leaving them alone without assistance.

Physical therapy.

And what can we do for the sick children? At every age we can make the movements of their muscles more flexible by a physical therapy treatment that is adjusted to the age, the cooperation, and the capabilities of the children. We also can stabilize and improve the respiration of the older child, and we can improve the mobility of the thorax. All of these are not cures, but they are therapies which can help delay the progress of the symptoms and the difficulties.

Technical aids.

An important aspect is without doubt that, in every age, the correct technical aids are available for the Duchenne child. We can be happy that in our western countries that we can afford this. We often see children from eastern countries where there are much larger financial problems than here, where it is quite impossible, e.g., to supply a child with an electric wheelchair because there is nobody who could pay for that. And even if someone would collect enough money, the wheelchair could not be serviced, so it does not make much sense to donate an electric wheelchair to a boy there. If you see the difference between the quality of life of these foreign children and our Duchenne boys, then one realizes how important it is that all these things, the availability of wheelchairs, standing aids, splints, etc., is so optimal that they really can improve the quality of life considerably.

Orthopedic operations.

Orthopedic operations are also important. Contractures of the extremities, above all of the legs, are part of the Duchenne muscular dystrophy, and they contribute to the loss of ambulation. One can operate them quite early, at the age of six, seven years, as Professor Forst is doing it here in Erlangen. Some children are afraid of the operations so that the families cannot decide about them so early. Then the operation can be done later but preferably just before the loss of ambulation so that the operation itself does not affect the walking ability in a negative way. At this time, one can maintain the standing ability of the children, e.g., in a standing aid or with the help of a raising mechanism of the electric wheelchair.

And finally the scoliosis operations, whose results convince me more than the operations of the contractures. When the Duchenne muscular dystrophy follows its

natural course and one does not like to do or cannot do anything for the curved spine, then this means that at the age of 17 to 20 years, the spine of most of the patients becomes curved, that this causes pain while sitting, and that an sitting upright in the wheelchair is not possible any more, and that in fact only some sort of half-lying in a reclining bed is possible. This does not allow participation in the social life, going out with the electric wheelchair, spending time with friends and going with them to restaurants, as many older patients I know are doing. The operation of the scoliosis in time makes all this possible again, because the spine remains stable and straight indefinitely, and the patient can again sit upright in his wheelchair for a longer time. Thus, the scoliosis operation has important social consequences, and it therefore is important for these patients.

There is general agreement now that the scoliosis operation should be recommended when the progressing spine curvature reaches 30 degrees. At this relatively small angle, the operation is shorter, less stressful and more successful than when one would wait much longer. After all, the operation will not be possible any more when the lung function has decreased to below 25% of normal. Thus, from this time on, the families have about one to one and a half years time to decide whether to have the operation performed or not.

Genetic counseling.

Genetic counseling right after the diagnosis, can contribute that the disease does not repeat itself in the same family. If, in addition, one could propose to the women who are related to the mother of the patient, that they also have to have genetic analyses in order to see whether they are carriers, then one could even avoid the first cases of Duchenne boys in their families

This is obviously an extremely important topic that never should be forgotten, and that has to be done for each affected family. Duchenne muscular dystrophy is a hereditary disease. It has not always been present in the family, 30% of the cases are caused by new mutations. But, obviously, that has to be carefully determined, one cannot solve this problem just by hoping that the boy's disease was a new mutation. One cannot take this for granted.

Unfortunately, as we cannot cure the disease, prevention is extremely important. This way, one could try to avoid that more children are born in the same family with this dreadful disease. Therefore, an early diagnosis is so important as soon as the first clinical symptoms appear, so that the family could be genetically counselled before the next child is expected.

And one should also not forget that the disease has this dangerous, sex-linked inheritance, that in addition to the mother of the sick boy, also other girls and women among their relatives can be genetic carriers. This is also true for the sisters of the patient and for the sisters of the mother and possibly for the grandmother and her sisters and their descendants, etc. So, under unfavorable circumstances, many women in an extended family can be carriers.

If all these women know about their risks, targeted family counseling can be offered. The present possibilities of prenatal diagnostics do not exclude carriers of having healthy sons. They must, however, have prenatal diagnoses

being made and then, if necessary, accept a termination of pregnancy. But this is also a difficult question to which every individual family, with the help of experts, has to find its own answer.

It is important also that it should be the pediatricians and family doctors who should explain to the families what kind of risk the relatives of the mother could have.

Nobody can expect that the parents with a Duchenne boy, even when they have informed themselves, understand the genetic consequences for their entire extended family. To explain this is the duty, above all, of the pediatricians who know the families, they have to inform them about everything.

But we, too, are responsible, even legally obligated, to send the families to a specialized geneticist who could inform not only the immediate family but also the relatives who might be at risk. This is without doubt the duty of every specialist who cares for these families.

Money for research.

As the last topic of this discussion, I would like to discuss the wish of many Duchenne families to collect money for research, and to cite a positive example: In November of last year, my friend, Dr. Klaus Klar, general practitioner in Achern, a small town near Baden-Baden, one evening recited by heart ballades of Schiller before 200 listeners. The result was 3,700 euros which all went to Dr. Judith van Deutekom in Leiden in Holland for research on exon skipping. But we know that the second clinical study there will cost about 800,000 euros. Dr. Klar and the other people now think that the amount they raised on this evening were "only a drop on a hot stone". Please tell the families at the end of this important interview that their efforts are not drops on a hot stone.

Prof. Dr. med. Rudolf Korinthenberg
Universitätskinderklinik Freiburg
Mathildenstraße 1
D-79106 Freiburg, Germany

Dr. rer. nat. Günter Scheuerbrandt
Im Talgrund 2, D-79874 Breitenau
E-Mail: gscheuerbrandt@t-online.de
Internet: www.duchenne-forschung.de

Duchenne families, who would like to receive regularly interviews and research reports, should send their e-Mail address to Dr. Scheuerbrandt

Research is expensive, mostly because it needs researchers and their helpers, over and over again and for a long time. It is not a question of funding expensive instruments, but paying for our assistants, our students and postdocs who perform the studies and who work from the morning till the evening. They are not just there, they must be employed and paid, and not only for a short time. At the university, we call that third-party funding. In addition to that, we try to get special funds for research for a therapy of Duchenne muscular dystrophy, in addition to the state funds which we are also getting.

For our prednisone-cyclosporin study we were quite successful, we got help from the German Duchenne parent project group "Aktion Benni & Co", from the German muscular dystrophy association, and from the Novartis company. With the public funds alone, which we have received from our Federal Department for Education and Research, we would not have been able to perform this study in the way that we feel is necessary

Thus, research needs large financial funds, and they often consist of many little donations. We cannot expect to obtain suddenly 500.000 euros from some company or from some other source. We always have to try to get many small donations from various groups, from private persons, from companies, and from associations, which add up to larger amounts with which we really can do things which would be impossible without that help. Aktion Benni & Co has shown that this really works. And it should go on this way, please!

Many thanks, Professor Korinthenberg, also on behalf of the many families, not only in Germany, who need this detailed information in this interview, so that they can help their sick children as much as possible.