

**REGISTER FOR
AUTOINFLAMMATORY DISEASES (AID)**

Information letter for adolescents \geq 14 years

Dear _____,

You have been chosen to participate in a large-scale study on autoinflammatory diseases (autoinflammatory diseases = AIDs) in childhood. These diseases are accompanied by repetitive episodes of fever and an inflammation activity which affects the whole body. These symptoms mostly disappear after some time. Fever might not occur in some cases. The diagnosis can be performed easier nowadays with genetic blood tests. Such a study has not yet been carried out in Germany. It is very important however for answering targeted questions regarding this disease group.

Why you? You have been chosen by your physician because your disease belongs to the autoinflammatory disease group (AID). This includes: genetically defined hereditary periodic fever syndromes (HPF) such as familial Mediterranean fever, hyper-IgD syndrome (HIDS), tumour necrosis factor receptor 1-associated periodic syndrome (TRAPS), Muckle-Wells syndrome (MWS), familial cold autoinflammatory syndrome (FCAS) and chronic infantile neurological, cutaneous, and articular (CINCA) syndrome or not yet genetically defined systemic onset juvenile idiopathic arthritis (SoJIA), the PFAPA syndrome (fever, mouth/throat inflammation as well as lymphadenitis) and further fever syndromes that have only been clinically defined until now.

Our **goal** is to increase our knowledge about AIDs. Since AIDs occur very rarely, we would like to find out more about them, and especially about how you are feeling under the treatment and over the course of the disease. How frequently do AIDs arise in childhood? Which complaints are there when disease begins? Which gene mutation leads to which symptoms? Which treatment is helpful? Which problems arise during treatment? Can newer medication also be used in childhood without hesitation?

What do we do? To start with, all participating children with AIDs are documented across the country via an online AID register at the time of diagnosis. For this purpose, your physician will fill out a questionnaire about your disease online.

Next, the known cases are documented after an outpatient or inpatient follow-up with the physician in the course of the disease, and this is also done online. Monitoring the course of the disease makes it possible to determine therapeutic success and failure and to draw conclusions from this for treatment. Each time you visit your physician, your current laboratory values, your state of health and your complaints are thus entered into the PC.

What is documented? The current forms (master data, diagnosis, follow-up and therapy) can be downloaded via the homepage of the AID register. The following information is asked for in these forms:

Master data: Month/year of birth, sex, encrypted patient code (PID)

Diagnosis: Diagnosis and genetic findings, anamnesis, symptoms and laboratory parameters before diagnosis confirmation

Follow-up: Size/weight, symptoms, laboratory values, therapy plus side effects

Therapy: Selection and dosages of medication



What do you get from participating in the study? You and your parents can put any questions regarding your disease to physicians who have a great deal of experience with children with the same problems. You can contact us on the following telephone numbers: Essen +49 (0) 201/723 3350 (Dr. Lainka, Dr. Neudorf) or Krefeld +49 (0)2151/322301 (Prof. Niehues). You can find further information on the Internet on the AID register homepage (www.AID-register.uk-essen.de).

Cooperation: There is a nationwide cooperation established with the DRFZ (German Rheumatism Research Center) in Berlin, which also collects data (core documentation in childhood) on patient history once a year.

This is dependent on your written agreement. We are hereby asking you to participate in the AID register. Participation is voluntary and can be cancelled at any time without giving reasons and without any disadvantages for your medical care. In the case of cancellation, the data that has already been collected will be deleted immediately.

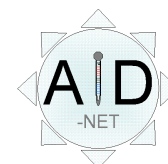
Data protection! All German paediatric clinics and all specialised outpatient clinics and laboratories are taking part in this research project. All data is treated with strict confidentiality. It goes without saying that neither your name nor your address will be mentioned anywhere. For the purpose of registration, your attending physician will assign a code number (PID) using a random number generator on a server. Only the physician can match your PID number to you. This is why this letter has been kindly passed on to you by your paediatric clinic. The data cannot be matched to you as an individual during data collection, processing or publication. All data is carefully kept and protected against unauthorised access. The data is processed exclusively in anonymous form. The results of the test will be represented in the form of summary tables.

Since data records are not always complete, we are asking for your permission to make further enquiries to your attending physician in our capacity of directors of studies (see above), in order to complete missing data

Thank you in advance for your cooperation.

Kind regards,

Dr. med. E. Lainka
Coordinating investigator



BIO BANKS FOR AUTOINFLAMMATORY DISEASES (AID)

Information letter for adolescents ≥ 14 years

Dear _____,

First we would like to thank you again for your willingness to take part in the register for autoinflammatory diseases. At present it is hard to gear the therapy to the disease activity. This is an important issue, because the therapy has to be geared to the actual seriousness of the disease. Neither too much nor too little medication is good for you. We do not yet have any references as to so-called risk factors that make a more serious course of disease likely. However, we have found in more recent studies that certain antibodies can be measured in the blood and that the values of these antibodies (MRP8/14 and S100A12) make a prediction possible. In the last years we have learned much about changes in genetic makeup that can lead to autoinflammatory disease. Nevertheless, in every second patient until now, none of the known genetic causes have been detected. It is therefore important to look for genetic changes that are thus far unknown. This can help to better predict the course of certain diseases and develop new therapies in the future.

What do we do?

In your case, the values for MRP8/14 and S100A12 are to be measured. At the time of the regular tests carried out by your physician, blood tests are performed if necessary. A blood sample is only to be taken here if a blood withdrawal is carried out anyway for medical reasons. No additional blood withdrawal is to take place for investigating inflammation proteins MRP8/14 and S100A12; only 4 ml (2 small tubes) extra are taken. If a blood test is carried out however, then it can be measured whether there is a risk of a more serious disease with inflammation proteins MRP8/14 and S100A12 as well as possible additional blood components. We would also like to ask you to provide a one-off blood sample from which DNA (the carrier of the human genetic formation) will be obtained. New genes that are important for the development of your disease can be researched using this DNA sample.

Who are we?

Prof. Dr. med. Dirk Föll works at the children's hospital of the university in Münster and is spokesperson of the "clinical studies" commission of the German Society for Paediatric and Adolescent Rheumatology. He already supervises the central sample bank for children and adolescents with rheumatism and has been working on the research of laboratory tests for inflammatory diseases for a long time. Dr. med. Helmut Wittkowski works at the children's hospital of the university in Münster and will supervise the sample bank for the register for autoinflammatory diseases. He has been working on the investigation of laboratory tests for inflammatory diseases for a long time, especially for autoinflammatory diseases. Address: UKM Kinderklinik, Albert-Schweitzer-Str. 33, 48149 Münster, telephone: 0251-83 56578, fax: 0251-83 56549, email: h_wittkowski@yahoo.de.

PD Dr. med. Johannes-Peter Haas works at the clinic for paediatric and adolescent rheumatology in Garmisch-Partenkirchen. He has been supervising the Genetic Biobank of the Society for Paediatric and Adolescent Rheumatology for several years and has already led several genetic studies. Address: Deutsches Zentrum für Kinder- und



Jugendrheumatologie, Gehfeldstr. 24, 82467 Garmisch-Partenkirchen, tel.: 08821-701117,
fax: 08821-701201, email: haas.johannes-peter@rummelsberger.net

This is dependent on your written agreement!

We are asking you to participate in this investigation so that we can arrange a purposeful and as low-risk a treatment as possible for the future. The data is collected exclusively in pseudonymous form as part of the research project. Even if you decide not to have test results documented, this will in no way affect your treatment. Revoking this agreement is possible at any time without giving reasons and will not lead to disadvantages for your further medical treatment. In the case of revocation, the data and samples that have already been collected will be destroyed on request.

Data protection

All German paediatric clinics and all specialised outpatient clinics and laboratories are taking part in this research project. All data is treated with strict confidentiality. It goes without saying that neither your name nor your address will be mentioned anywhere. The data cannot be matched to you as an individual during data collection, processing or publication. All data is carefully kept and protected against unauthorised access. The data is processed exclusively in anonymous form. The results of the test will be represented in the form of summary tables.

Thank you very much in advance for your cooperation.

Prof. Dr. D. Föll

Dr. H. Wittkowski

PD Dr. J.P. Haas

- Coordinating investigators -