Spotlight on...

Interview with: Dr. Gabriela Pohla-Gubo, expert in Epidermolysis Bullosa

Epidermolysis bullosa (EB) encompasses a group of disorders characterised by recurrent blister formation as the result of structural fragility within the skin and other tissues. All types and subtypes of EB are inherited and rare. EB affects individuals from all ethnic origins and there is no gender predilection. Clinical manifestations range widely, from localised blistering of the hands and feet to generalised blistering of the skin and oral cavity and injury to many internal organs.

In September 2009, the International Epidermolysis Bullosa Research Conference took place in Vienna, Austria, bringing together some 70 experts from 14 different countries to review the latest achievements in research and care for EB. This conference can be viewed as a model, illustrating how rare disease collaboration and cooperation in the field of research and treatment can be organised. Present at the conference was Dr. Gabriela Pohla-Gubo, PhD, a co-founder of patient organisation DEBRA-Austria, Head of the Laboratory for Immunology and Allergology at the Department of Dermatology, General Hospital, Salzburg, and Head of the EB Academy at the EB House Austria.

OrphaNews Europe talks with Dr. Pohla-Gubo about the outcome of the conference and the current state of knowledge and resources for this group of rare diseases:

OrphaNews Europe: The 2009 DEBRA International Epidermolysis Bullosa Research Conference, organised by patient support organisation DEBRA, brought together a large
number of specialists from different geographical regions and different areas of expertise. What were the overarching goals of the conference and how does such a conference help to move forward research?

**Gabriela Pohla-Gubo:** The conference sought to review progress in and barriers to fundamental EB research, and the development of clinical solutions; to consider research aspects of EB not addressed to date; to identify unexplored opportunities and relevant research from complementary areas; and to arrive at a community consensus on research and development priorities. The conference encourages and facilitates researchers to work together to exchange experiences and share knowledge and resources.

**OrphaNews Europe:** Approximately how many different subtypes of EB have been identified?

**Gabriela Pohla-Gubo:** There are four primary disease groups: EB simplex, junctional EB, dystrophic EB, and Kindler syndrome. Within these groups there are more than 30 clinical pictures, depending on the specific mutation. As a group, EB affects one in 17,000 persons.

**OrphaNews Europe:** To date, how many genes have been implicated?

**Gabriela Pohla-Gubo:** There have been 14 genes identified. However, even within the same genotype there can be many different phenotypes, each presenting a different outcome.

**OrphaNews Europe:** In what percentage of cases is the disease clinically apparent at birth?

**Gabriela Pohla-Gubo:** All forms are apparent at birth.

**OrphaNews Europe:** In general, what is the prognosis for this group of diseases?

**Gabriela Pohla-Gubo:** It all depends on the form. For example, the Herlitz type of junctional EB typically ends in mortality at age one or two years. Patients usually die from sequelae like sepsis or cancer. The recessive dystrophic EB usually results in a very aggressive form of squamous cell carcinoma and patients usually die around age forty.

**OrphaNews Europe:** Can you discuss pain management?

**Gabriela Pohla-Gubo:** Pain management is a major part of clinical treatment. The blisters are very painful – especially when they occur in the mouth, the eyes or the oesophagus, for example. Changing the dressings is also a very painful procedure and can take up to three hours. The dressings are typically changed by parents – who are taught how to do this, and who make the best nurses for the patients.

Itching is also a very severe problem. Some patients are unable to sleep because the itching is so distracting and common itching drugs are less effective. Additionally, there can be digestion and malnutrition problems when children are unable to swallow due to painful
constriction of the oesophagus caused by blisters and scars.

**OrphaNews Europe:** Can you comment on some of the therapeutic options under development? Which seem most promising at this time?

**Gabriela Pohla-Gubo:** One treatment that has demonstrated proof-of-principle is a grafting approach using an *ex vivo* gene therapy. Such a treatment was performed in 2006 on one patient in Italy who has junctional EB due to a laminin 332 gene mutation. To date (four years later) the grafted skin areas continue to express sufficient functional laminin. This therapeutic approach is indicated for certain severe wounds that do not heal and are long-lasting. It is particularly important as such wounds often become cancerous. Austria is currently petitioning regulators to conduct a similar trial on a patient and our hope is to move forward in the near future.

**OrphaNews Europe:** Compared to other rare diseases, would you say there is much interest on the part of the biopharmaceutical industry in developing treatments for this group of diseases?

**Gabriela Pohla-Gubo:** Not really at this time. Some small trials are underway for the less severe dominant forms of EB involving small interfering RNAs that could potentially be used in creams.

**OrphaNews Europe:** Can you describe the Epidermolysis Bullosa House Austria?

**Gabriela Pohla-Gubo:** The EB House was created five years ago by patient organisation DEBRA Austria in collaboration with physicians and other professionals. It is a model for a centre of expertise and we fulfil the criteria set out by the European Commission's Rare Disease Task Force for such a centre. We have developed a state-of-the-art clinical centre, a research centre, and an academy in order to teach families and professionals. We hope to become an official centre of expertise, though we do not yet have legal recognition as such. We are unique in Europe – there are other EB specialist centres, but they do not offer all three of the elements that we do.

Our centre has two specialised doctors and two specialised nurses. As most EB patients live at home, we offer education for families – some of whom come for a full day of training and information. Physicians from abroad are also invited to come and learn. We have also had patients from 15 different countries to date. This has been very positive, though there have been some problems with reimbursement. Patients from the EU countries are asked to bring an E112 form for reimbursement. This form is specifically for patients with a known disorder.

Another thing we would like to do is create a European registry. Austria has had a registry for more than ten years. We have 300 patients in our registry, of whom one hundred come from abroad. We experience a good level of cooperation from local physicians as well as patients and families living abroad.
**OrphaNews Europe:** Is pre-natal screening routinely offered to families with an affected member?

**Gabriela Pohla-Gubo:** Yes, particularly at the EB House Austria and in the EU countries where specialised centres for EB (e.g. Germany, UK) have been established. Less developed countries do not have these resources.

**OrphaNews Europe:** Could you discuss how the disease is managed in developing countries?

**Gabriela Pohla-Gubo:** It is very difficult. We have heard reports from places such as South America where patients are obliged to cover their wounds with newspaper. However, we are starting to collaborate more and more with these countries. The patient organisation DEBRA is active in more than 40 countries now. Chile developed the second EB House in the world and Croatia is offering a place for families to stay during patient treatments at the clinic. Other countries – in particular, Poland – have expressed interest in building a structure similar to the EB House in their country. Mexico is also trying to develop specialised resources. For participation in the 2009 DEBRA International Epidermolysis Bullosa Research Conference, we were able to cover the costs of some attendees who did not have the funds. When we first got started, we had a lot of help, particularly from DEBRA UK, which is thirty years old now. We believe it is now our turn to try and aid other countries, especially the new EU members in Eastern Europe.

Read a summary of the 2009 DEBRA International Epidermolysis Bullosa Research Conference

Consult the Journal of Investigative Dermatology article on the 2009 DEBRA International Epidermolysis Bullosa Research Conference (available via the DEBRA International website)

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