It is anniversary time!
It is now 20 years ago that Dr D’Angio arranged a workshop in Philadelphia (May 16, 1985) with a small group of 15 colleagues interested in the histiocytoses. That meeting became the foundation of the Histiocyte Society, which now is a vivid organization with treatment protocols available in most pediatric hematology/oncology units worldwide. Thank you Dan for your initiative and for all you have done to help the Society since then!

Soon thereafter, in 1986, the Histiocytosis Association of America (HAA) was created by Jeff and Sally Toughill. This nonprofit organization for patients and families has the goal to promote scientific research into the histiocytoses, to offer support to patients and their families, and to promote education related to the histiocytoses; in addition it serves as the administrative office for our Histiocyte Society. Thank you Jeff and Sally for your initiative and all your support through 20 years, and warm thanks also to Beth Miller at the office for all your assistance and care!

So what has been achieved?
I find that a lot has been accomplished and we all can be proud! We have had tremendous success in many of our endeavors. The Histiocyte Society treatment protocols are now available in most pediatric hematology-oncology centers worldwide. This way children get the same therapy worldwide; a therapy that can be considered the golden standard of today for both LCH and HLH.

Moreover, with regard to HLH, survival has improved markedly with our treatment protocols, and the biological HLH studies have revealed three causative genes and the most exciting biological news with insights into the life and death of cells in a system vital for human survival. We have been very fortunate. Now I hope the time has come for LCH and with an increasing survival and improved life of the survivors. In the same way as was the case with HLH, I hope that understanding the underlying biology causing LCH may be of central relevance to human biology.

The Vancouver Annual Meeting
I found the 21st Annual Meeting in Vancouver very exciting - and in a most beautiful city. There were many attending the meeting, a new record on the American continent, another sign of the vigor of the Society. The invited speakers all contributed to subsequent vivid discussions, and some presentations were highly praised afterwards by many colleagues. I hope they will initiate new thoughts and new roads of research.

In addition, there was so much important news delivered by our members, ranging from biological studies, such as a presentation of the third gene causing FHL (syntaxin-11), to clinical studies, such as many important studies on late effects of LCH and HLH. I find that the research in many ways has entered a higher level as compared to when I first attended the meetings. The clinical studies are larger and more sophisticated, and the biological studies are clearly also more advanced. I do hope this will result in better therapies for the affected patients in the near future.

Welcome to Buenos Aires!
I would like to thank all of you that came to Vancouver for making the meeting a success. The next meeting will be in Buenos Aires (the main meeting will be October 15-17, 2006), and I am sure that Jorge Braier and his team will arrange a very exciting meeting! Start to plan your participation now, and take the opportunity to see something outside of the conference hall as well!

There are still many exciting problems awaiting a solution. Let’s continue to work hard to try to solve them! Work, Think, Work, and Think again, be it with patient care, clinical science or basic science (or a combination)! Small steps and big steps forward are all important. And join us in Buenos Aires to listen to others experiences or share your own findings!

MESSAGE FROM THE PRESIDENT
## HISTIOCYTE SOCIETY EXECUTIVE BOARD 2005—2006

<table>
<thead>
<tr>
<th>Position</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>President</td>
<td>Jan-Inge Henter</td>
</tr>
<tr>
<td>President-Elect</td>
<td>Alexandra Filipovich</td>
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<tr>
<td>Treasurer</td>
<td>Nicole Grois</td>
</tr>
<tr>
<td>Secretary</td>
<td>James Whitlock</td>
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<tr>
<td>Member-at-Large</td>
<td>Vasanta Nanduri</td>
</tr>
<tr>
<td>Member-at-Large</td>
<td>Carlos Rodriguez-Galindo</td>
</tr>
</tbody>
</table>

## HISTIOCYTE SOCIETY EDUCATION COMMITTEE

<table>
<thead>
<tr>
<th>Position</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milen Minkov, Chair</td>
<td>Kim Ericson</td>
</tr>
<tr>
<td>Kevin Windebank</td>
<td>Naoko Kinugawa</td>
</tr>
<tr>
<td>Kim Nichols</td>
<td>Joseph Neglia</td>
</tr>
<tr>
<td>Julio Goldberg</td>
<td></td>
</tr>
</tbody>
</table>

## HISTIOCYTE SOCIETY STUDY GROUPS

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Chairperson</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLH</td>
<td>Jan-Inge Henter</td>
</tr>
<tr>
<td>Epidemiology</td>
<td>H. Stacy Nicholson</td>
</tr>
<tr>
<td>CNS</td>
<td>Nicole Grois</td>
</tr>
<tr>
<td>LCH-S</td>
<td>Jean Donadieu</td>
</tr>
<tr>
<td>LCH III</td>
<td>Helmut Gadner</td>
</tr>
<tr>
<td>Adult Histioctosis</td>
<td>Maurizio Aricò</td>
</tr>
<tr>
<td>Pathology</td>
<td>Ronald Jaffe</td>
</tr>
<tr>
<td>Malignant Histioctosis</td>
<td>Peter Bucsky</td>
</tr>
<tr>
<td>Late Effects</td>
<td>Riccardo Haupt</td>
</tr>
</tbody>
</table>

## ANNOUNCEMENTS

### ANNUAL MEETING

The 22nd Annual Meeting of the Histiocyte Society will take place in Buenos Aires, Argentina. The preliminary schedule will be as follows:

- **Friday, October 13**
  Executive Board Meeting

- **Saturday, October 14**
  Committee and Study Group Meetings

- **Sunday, October 15 - Tuesday, October 17**
  Annual Meeting Sessions

- **Wednesday, October 18**
  Special Symposium

Active members of the Histiocyte Society will be sent meeting registration information in March 2006. All other interested parties should contact the Office of the Secretariat for materials.

### ADDRESS UPDATES

Please keep your contact information current; submit any changes (particularly email changes) to the Office of the Secretariat.

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The 21st Annual Meeting of the Histiocyte Society was held in Vancouver, British Columbia, Canada at the Sutton Place Hotel, September 25-27, 2005. There were 119 attendees. Several registered members were unable to attend due to travel restrictions related to Hurricane Rita in the US Gulf Coast area. The meeting was called to order by President Jan-Inge Henter at 5:02 p.m. on September 26, 2005.

Secretary’s Report

Dr. Filipovich asked for a motion to approve the minutes of the 2004 General Assembly meeting. After correction of an error in the results of elections (Drs. Kevin Windebank and Julio Goldberg were elected to the Education, not Scientific committee), the minutes were approved.

The list of potential new members of the Society was presented to the members at the General Assembly:

Itziar Astigarraga
Hospital De Cruces
Barakaldo, Bizkaia Spain

Fadi Braiteh
University of Texas, MD Anderson
Houston, Texas USA

Girish Dhall
Children’s Hospital at St. Peter’s University Hospital
New Brunswick, New Jersey USA

Hüseyin Engin
Karaelmas University Faculty of Medicine
Zonguidak, Turkey

Michael Jeng
Stanford University School of Medicine
Palo Alto, California USA

Michael Maschan
Russian Children’s Clinical Hospital
Moscow, Russia

Akira Morimoto
Kyoto Prefectural University of Medicine
Kyoto, Japan

Hubert Mottl
University Hospital Motol
Prague, Czech Republic

Georg Seifert
Charite-Universitatmedizin Berlin
Berlin, Germany

Matthew Ming Kong Shing
Prince of Wales Hospital
Hong Kong, China

Ikuyo Ueda
Kyoto Prefectural University of Medicine
Kyoto, Japan

Wendy Wong
Stanford University
Palo Alto, California USA

The membership unanimously approved the applicants and congratulated new members.

Treasurer’s Report

Dr. Grois reported that the Society finances were in good balance. The majority of revenues come from membership dues and meeting registration fees. As of September 26, 2005, 30 members had not paid their dues, despite repeated reminders. As has been done in the past, a list of non-dues paying members will be listed at the Annual meeting.

Dr. Grois reported that the number of attendees, in particular medical professionals, has been relatively stable over the past several years.

President’s Report

Dr. Henter outlined plans for the next annual meeting in Buenos Aires, Argentina on October 15-17, 2006. The meeting will be accompanied by satellite symposia in Immunodeficiency and Oncology. It is anticipated that the registration fee will be lower than in recent years, due to lower costs of the meeting venue.

Dr. Henter again mentioned the formation of the registry of Rare Histiocytic Disorders. The details are being finalized by Drs. McClain and Weitzman.

Dr. Henter informed the members that the HAA Board had offered to pay for a consultant to review the data collection and management infrastructure for the HS clinical studies to assess need for improvements.

Dr. Henter emphasized the importance of informing our colleagues in internal medicine about Histiocytoses and engaging them in clinical practice of these diseases.

Dr. Henter solicited comments about this year’s format for poster presentation from the audience.

Continued on next page
Dr. Henter reported that it is currently anticipated that LCH III will complete accrual in 2008. Dr. Gadner will then step down as chair. New ideas and recommendation for leadership of LCH 4 should be considered soon.

Dr. Henter reported that the Board has been developing operating guidelines for opening new clinical trials, formation of writing committees and a policy for access to data collected by clinical trials for other research. Since there was not enough time to discuss the guidelines in any detail, members of the audience requested that the drafts be circulated to the membership for comments after the meeting.

Dr. Henter reported that the process of HAA grant review will be improved. One of the Board’s members-at-large will serve as liaison to the Scientific Committee to ensure standardization of approach to grant reviews over the years. The HAA grant deadlines are: November 15, 2005 for electronic submission from investigators, and announcement of funding by December 31, 2005.

Dr. Henter recommended expanding the membership of the Education Committee to a total of seven members. After some discussion this was approved.

Dr. Jean Donadieu presented the report from the Scientific Committee, and Dr. Ricardo Haupt discussed the several initiatives of the Epidemiology and Late Effects Committee (see below). The report from the Education Committee was not presented at the General Assembly, but can be found elsewhere in this publication along with the other committee reports. Dr. Henter thanked Dr. Maurizio Aricó for his excellent work as chair of the Education Committee over the past several years.

**New Business**

Dr. D’Angio congratulated the participants on an excellent meeting overall. He also pleaded for standardization and clarity in the format of PowerPoint presentation – as he found some of the animation distracting.

Dr. Ladisch spoke briefly about the project for engaging a consultant, paid by the HAA, to examine strategies for support of infrastructure (data management and running of clinical research) underlying the HS clinical trials.

Dr. Henter urged the Scientific and Education Committees to choose chairs within the next 2 weeks.

Dr. Gadner and the audience thanked Dr. Dan D’Angio warmly for his foresight in organizing the inaugural HS meeting 20 years ago.
**COMMITTEE AND STUDY GROUP REPORTS**

**EDUCATION COMMITTEE REPORT**
*Submitted by Maurizio Aricò*

During the last year, the main activity of the EC was to contribute to the development of the meeting program and then to evaluate the abstracts submitted. The abstracts have been collected as usual by the HS Secretariat and then circulated among the EC members for blinded scoring. Afterward, the Secretariat collected and averaged the scoring in an overview, which formed the basis for attribution of the papers to the different sessions. Given the number and quality of the contributions, none of them had to be rejected.

**SCIENTIFIC COMMITTEE REPORT**
*Submitted by Jean Donadieu*

The scientific committee has evaluated this year 22 applications submitted following the call for projects from the Histiocytosis American Association.

Three applications were focused on clinical research (including 2 clinical trials approved by the HS) and 19 were focused on basic research. Seventeen and five projects were focused on Langerhans cell histiocytosis and familial lymphohistiocytosis.

Each member of the scientific committee has ranked the projects. If a member was committed in a project, he was not allowed to rank it.

The evaluation was quite difficult. The difference between projects, in term of the overall scores (the addition of the score of each member) was quite small at the end of the process. Overall, about two third of the projects were pertinent, feasible, and would deserve to be granted. However we need to take a decision and the 4 best projects were selected and granted by the HAA.

The four granted projects were:
1) A new transgenic mouse model for skin LCH probing the disease mechanisms / Dr Acha Orbea Swiss
2) Novel photoconvertable fluorescent proteins to trace hemophagocytes in whole blood / Dr Schneider - Germany
3) Development of murine model for LCH using binary knock-in mice - France
4) Genetic characterization of LC differentiation in LCH Dr Lee FL - USA.

The Scientific committee wishes for all these projects a very successful outcome and also wants to transmit to the unsuccessful applicants encouragement to find other funding and to realize their projects.

**LCH-BMT STUDY GROUP REPORT**
*Submitted by Maarten Egeler Co-Chair*

The primary objective of a Stem Cell Transplantation (SCT) protocol for the most extreme form of Langerhans cell histiocytosis is to determine the outcome of a “reduced intensity hematopoietic SCT” with respect to disease control and survival. Secondary objectives are to evaluate and to determine regimen-related toxicity like graft-versus-host disease, engraftment as well as the possible difference in outcome with respect to a matched sibling donor versus an alternative donor.

Eligibility: Patients with multisystem disease with involvement of one or more risk organs, who have progressive disease after treatment with LCH-I, LCH-II or LCH-III as well as the current salvage protocol. Patients with the same clinical characteristics treated with equivalent treatment modalities will be enrolled as well and might be evaluated separately.

The conditioning regimen is Campath, Fludarabine and Melphalan based. The protocol has been approved by the Scientific Committee of the Histiocyte Society and will hopefully officially been opened in January 2006. Together with a group of colleagues, transplanters outside the Histiocyte Society as well as devoted LCH physicians we have come up with a regimen that we feel to be excited. Dr. Scott Baker will take over the baton as Chair of this Committee.

**MALIGNANT DISORDERS STUDY GROUP REPORT**
*Submitted by Peter Bucsky, Chair*

Over many years, till now, no children and adolescents have been reported for the Malignant Disorders Study Group with some kind of malignant histiocytic disorders. However, the study group does still exist and would like to work with engagement and pleasure!

Please report such patients by all means either at our Society or contact me directly in the next year (E-mail: bucsky@paedia.ukl.mu-luebeck.de).

Should not be reported such patients next year, we have to consider closing this study group.

So I ask you cordially to help this group and thank you for it already in advance.
HLH STUDY GROUP REPORT
Submitted by Jan-Inge Henter, Chair

Members: J-I Henter (Sweden, Chairman), M Aricò (Italy), M Egeler (the Netherlands), A Filipovich (USA), AC Horne (Sweden), S Imashuku (Japan), G Janka (Germany), S Ladisch (USA), K McClain (USA), V Nanduri (UK).

The HLH Study Group is mainly aiming at improving diagnosis and treatment for patients suffering from FHL/HLH. We also want to improve knowledge on the biological mechanisms causing the disease. The HLH-94 treatment protocol has been a therapeutic success. It has also provided a lot of research data, in particular on NK-cell activity in HLH. Importantly, during the last year one more gene causing familial HLH was reported, the syntaxin-11 gene. There are now altogether three known genes causing FHL, perforin, hMunc13-4 and syntaxin-11.

HLH-94
The HLH-94 protocol was closed for new patients by Dec 31, 2003, but is open for further reports of patients that initiated their HLH-94-therapy prior to that date. The protocol has been effective and appreciated. Most patients registered are from Europe and Japan. The outcome of the patients recruited the first four years is around 50% (around 75% survive until BMT, and around 65% survive the BMT) as published in Blood 2002 Oct; 100: 2367-2373.

Detailed analysis of patients that underwent SCT 1995 - 2000 (n=86) have been published recently (Br J Haematol 2005;129:622-30). The overall estimated 3-year-survival post-SCT was 64% (95% confidence interval ±10%) (n=86); 71±18% with matched related donors (MRD, n=24), 70±16% with matched unrelated donors (MUD, n=33), 50±24% with family haploidential donors (haploidential, n=16), and 54±27% with mismatched unrelated donors (MMUD, n=13). It is concluded that a) family haploidential donors and mismatched unrelated donors provide an acceptable outcome if no other donor is available, b) the survival curve is almost flat after the first year after SCT, and that survival is better in patients with non-active disease at SCT, but active disease should not automatically preclude SCT.

HLH-2004
A new protocol has been developed, and it was opened Jan 1, 2004. There are only minor alterations in the treatment regimen, one important change is that cyclosporin A is initiated at onset of therapy instead of after 8 weeks. In addition to the treatment protocol itself, biological studies on genetics and cytotoxicity will be associated with the protocol. In addition to the study subcenters (Scandinavia, Germany, Benelux, United Kingdom, Italy, USA and Japan), local coordinators for Spain (I Astigarraga), Austria (M Minkov) and South America (J Braier) are associated with the new protocol. Although we hope the results will be even better than the HLH-94 results, it is to early to draw any conclusions on the outcome of this treatment protocol.

ADULT STUDY GROUP REPORT
Submitted by Maurizio Aricò

At the Vancouver meeting the Adult Study group joined. The main issue was to update the procedures of start-up of the first prospective diagnostic and therapeutic trial for LCH in adults, denominated LCH-A1.

The study group is not yet fully complete because some countries are still on the way to identify their local coordinators. Nevertheless, several countries are represented most by both, hematologists and pulmonologists:
- Argentina (Blanca Diez),
- Austria (Michael Girschikofsky and Kurt Aigner),
- France (Thierry Généreau and Abdellatif Tazi),
- Germany (Claus Doberauer and J. Fichter),
- Italy (Maurizio Aricò and Emanuela De Juli),
- Netherlands (Arjan van de Loosdrecht and R.E. Jonkers),
- Norway (Geir Tjonnfjord and Finn Wesenberg),
- Russia (Elena Lukina), and
- U.S.A. (Kenneth McClain and Robert J. Arcucci).

The UK group met recently and identification of the contact person is on the way.

The state of activation is the following:
- Argentina—Unknown;
- Austria—Started;
- France—recognized as national protocol and partially granted.

Some delay with the IRB:
- Germany—waiting for insurance and IRB,
- Netherlands—Unknown,
- Norway—Unknown,
- Russia—Unknown,
- U.K.—Not yet started
- U.S.A.—Not yet started, and
- Italy—Started.

So far nine patients have been enrolled in Italy, one from Thailand and one from Sweden.

Clearly there is much room to improve the effort put in most countries to speed-up the procedures of start of the study.
A new protocol dedicated for the rare patients with LCH, multivisceral diseases, and failure to standard therapy has been adopted by the salvage therapeutic group of the Histiocyte society at Vancouver, September 25th. Why a salvage protocol LCH is commonly NOT a life threatening disease. But some involvements could be life-threatening. Roughly, it is possible to distinguish short term poor outcome, where the disease has a large extension, including a hematological dysfunction, and long term bad outcome, where the progressive destruction of a vital function (lung/ liver/ neurological function) may be deleterious. This protocol is dedicated very specifically to the first situation, and only in case of a frank failure to the standard regimen in LCH as proposed in the LCH3 protocol, associating at least vinblastine and steroid. This situation actually represents until now about 2/3 of the deaths observed in LCH until now. Therefore, the target for the salvage protocol is to improve the vital prognosis of this group of patients.

The rationale of this protocol is the report from the French group of a group of 10 babies in this very poor situation (1). This pilot study is now published in the European journal of cancer, presented by an editorial from S Weitzman and J Pritchard (2) which extensively developed the goals and the difficulty of this approach. In this pilot study, 7 babies where cured by the association of 2 Cda and Ara-C. In the same time, additional patients were reported as oral presentation at the last HS meeting (Vancouver sept 2005), both from the French group, but also by a russian’s team, while some cases were occasionally successfully treated in various centers worldwide. Despite a very high toxicity of this regimen, which have to be administrated ONLY by in a team trained in the management of myeloblastic leukemia’s protocol, the long term results were unexpected and promising until now (‘crude’ survival rate about 80%), as in this group of patients, no more than 20% of the patients were expected to survive until now.

Therefore, after many exchanges, the salvage therapeutic group of the HS has found an agreement to organize an open-labeled, non randomized, phase II study, which aim to demonstrate, in a large scale, that this therapeutic option is worth.

The manuscript of the protocol is finalized, approved by the scientific committee and now the protocol is in the administrative process, seeking to obtain official advice from an ethic committee (IRB) in EU as well in North America. The official opening of the protocol is planned to the beginning of 2006 and the protocol is planned to include 30 patients in a 4-year period.

Quote from Editorial in EJC (ref 2):

The aim of this study was to assess the efficacy and adverse effects of 2-chlorodeoxyadenosine (2-CdA) and cytosine arabinoside (Ara-C) in children with refractory Langerhans cell histiocytosis (LCH) and haematopoietic dysfunction. Ten patients, with a median age at diagnosis of 0.5 years, were enrolled in this study. Treatment comprised at least two courses of Ara-C (1000mg/m2/d) and 2-CdA (9mg/m2/d) administered for 5d every 4 weeks; subsequent median follow-up was 2.8 years (range 0.03-6.4 years). Among the 7 patients who received at least two courses of therapy, disease activity decreased in 6 patients, and control of disease was achieved in all patients after a median delay of 5.5 months. All patients suffered World Health Organisation (WHO) grade 4 haematological toxicity. Two septic deaths occurred shortly after administration of the first course of 2-CdA/Ara-C; a third patient was withdrawn from the trial after the first course and subsequently died following haematopoietic stem cell transplantation. This series is small, but we conclude that 2-CdA and Ara-C combined chemotherapy has major activity in childhood refractory Langerhans cell histiocytosis.
LCH STUDY GROUP REPORT
Submitted by N. Grois, CNS- Study Chair


Guests: K. Beutel, L. Filipovich, R. Haupt, V. Nanduri, C. Rodriguez-Galindo, J. Whitlock,

LCH III STUDY
PRELIMINARY RESULTS AND PROBLEMS
Patient recruitment has improved over the last year. After a study period of 53 months, 737 patients were enrolled onto the study by August 30, 2005. 315 patients were multisystem patients. 157 (50%) patients were “RISK” patients, and 158 patients were “LOW RISK” patients. 422 patients were single system patients.

LOW RISK GROUP
The primary study endpoint for Low Risk patients is the frequency of reactivations after 6 months of therapy comparing the 2 treatment arms with 6 months versus 12 months continuation therapy duration. In 154/158 patients of the “Low Risk Group” information at week 6 was available. 102/154 patients were responders (NAD/AD better), but only 73 of these (71%), in 27 patients the response was not specified, but still 13/ 27 were randomized. In 24 patients the response was reported as intermediate or worse but a randomization had been performed in 8/24. This is clearly against the instructions of the protocol and these patients are not eligible.

Response at week 6 might be difficult to assess in bone lesions. An unchanged bone lesion on x-ray does not preclude a “better” response, in case of clear clinical regression of signs and symptoms (pain, swelling, motion deficit).

Overall 94 Low Risk patients (61%) were randomized and this rate is still lower than the expected randomization rate of 72%. The time of randomization was at a median of 6.4 weeks after treatment start. In 18 patients the randomization was done too early, i.e. before week 5. In 28 patients the randomization was done too late, i.e. after week 9, in 2 of these even after week 26! This is clearly against the study rules. Unless there is an improvement of the rate of erroneously randomised patients, this error-rate will deteriorate the quality of the trial and compromise the whole study.

No randomisation in Low Risk Patients should be performed in the national sub-centers unless eligibility (i.e. response NAD/Ad better at week 6) is proven. The time of randomisation must be between week 6 and 12. No earlier and later randomisations will be accepted.

Of the 94 randomized Low risk patients, 8 are not eligible because they were randomized erroneously, but were nonresponders. For 6 of the remaining 86 patients, it is still too early to be included in the analysis for reactivation frequency after 6 months. 11 patients experienced a reactivation within the observation period. But 76 patients would be evaluable. However information is only available in 51 patients. In 33% follow up information is missing!

Considering the current patient accrual with 20-30 randomizations done per year the needed final sample size of 148 patients will be reached by the end of 2008.

Complete follow up information over the complete observation period (> 6months!! after therapy stop!!) is essential to be able to answer the question of the impact of therapy duration on the frequency of reactivations in Low Risk patients and also the secondary study endpoints (permanent consequences).

RISK GROUP:
The primary study endpoint for Risk patients is the frequency of nonresponse in risk organs at week 12 comparing the 2 treatment arms with 2 drugs (vinblastine + prednisone) versus 3-drugs (vinblastine, prednisone+methotrexate). 157 risk patients were reported and 134 randomizations were performed (85%). The response in risk organs ant week 6/12 is available in 92/124 (74%) evaluable patients (10 patients still too early). In 32 patients (26%) no information was reported. Complete follow up information over the observation period is only available in 54% of the evaluable patients!

Complete follow up information on the response rate but also on the complete observation period is essential to be able to answer the primary (response week 6 and 12) and secondary study goals (survival, reactivations, permanent consequences).

Nine deaths were reported. This is in keeping with the stopping rules of the study that require a 12-week death rate < 10%. Only 53/124 (43%) of randomized Risk patients
have complete toxicity data reported. 42% of the patients have no toxicity data reported at all.

The tremendous incompleteness of data compromises the implementation of the stopping rules. According to the study protocol deaths and severe adverse events (Grade 3/4) must be reported immediately to the study center within 48 hours.

Considering the current patient accrual with 30-35 randomizations done per year the needed final sample size of 228 patients will be reached by the end of 2008.

PLANNING FOR THE LCH IV STUDY

FORMATION OF A NEW STUDY COMMITTEE
In accordance with the new guidelines of the Histiocyte Society for the initiation of new studies, it was announced that new interested Society members who would like to contribute in the forthcoming LCH IV study committee should contact H. Gadner, as the Chair of the ongoing LCH III study.

The members of the potential new LCH IV committee will be appointed by the old committee in accordance with the HS Board.

FUTURE OF THE HISTIOCYTE SOCIETY DATABASES

Stephan Ladisch brought forward a request by the HAA to reconsider the feasibility and efficiency of the current data capture systems in use for the various Histiocyte Society Studies. An independent professional expert will be appointed to evaluate the current status and to elaborate a proposal for the most useful and economic way to organize data center(s) for the HS Studies.

LCH CNS STUDY GROUP REPORT

Study Group Members: J. Donadieu, N. Grois, J.-I. Henter, V. Nanduri


The LCH CNS 2003 protocol was released in June 2003 and constitutes a continuation of the LCH CNS 2000 study in a condensed version. It is the goal of the study to implement a uniform diagnostic program, to collect information on the natural history and pathophysiology of the disease, and on the outcome of patients treated with various therapeutic approaches. The recommendations for the diagnostic program include magnetic resonance imaging (MRI) to be done once/year (more frequently in case of tumorous lesions), motor efficiency tests and neurophysiological tests (brain stem evoked potential, visual and event related potentials) to be done once/year, psychometric tests every 2nd year, endocrine evaluation as clinically indicated. No guidelines for specific therapy are included in the protocol at this point.

By August 2005, 99 patients with neurodegenerative CNS disease were registered at the Study Center, however in only a minority of these patients complete diagnostic evaluation according to the protocol is reported: Neurological examination (EDSS, ARS) in 31 patients, psychological tests 27 patients, electrophysiological tests 17 patients. Only 11 patients have all 3 types of test reported at one time period. Follow up investigations are reported even less.

To assess the efficacy of whatever type of therapy given to patients with neurodegenerative CNS disease within a given patient, and to be able to compare the various regimens given to different patients, it is essential to evaluate all patients with neurodegenerative disease in a comparable way, as given in the guidelines of the CNS study protocol.

The increasing number of patient inquiries asking for treatment advice over the past year registered at the study center and also by other members of the CNS study group provides evidence for the need of uniform guidelines of the CNS Study Group of the Histiocyte Society for such patients, even when a standardized study at this point is not feasible due to the heterogeneity and rarity of the disorder.

An interim CNS LCH working meeting is planned for spring 2005 to establish uniform guidelines for the therapy in neurodegenerative disease, and to discuss further basic research projects.
ANNUAL MEETING

IMAGES OF VANCOUVER
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HISTIOCYTE SOCIETY CONSTITUTION

Article I: Name
The name of the society shall be the “Histiocyte Society”. This is a non-profit organization duly registered in the United States of America.

Article II: Aims
1. To improve the state of knowledge of the histiocytic disorders and the welfare of patients with these disorders and their families.
2. To promote, facilitate and carry out research in histiocytic disorders.
3. To facilitate and provide a forum for health professionals for effective communication concerning these aims.
4. To promote education and to educate physicians, nurses, other health professionals, scientists, legislators, and other lay persons in matters related to the histiocytic disorders.
5. To advise lay organizations in educational and other matters concerning histiocytic disorders.
6. To collaborate with other organizations with common aims.

Article III: Amendments and Revisions
1. Changes may be made by an affirmative vote of two-thirds (2/3) of a quorum at a general meeting of the Society, provided proposed changes have been submitted to and approved by the Board and circulated among the members at least one (1) month prior to the general meeting.
2. Proposed changes may originate with any ordinary member of the Society. They should be submitted to the Secretary at least two (2) months prior to the general meeting.
3. Changes properly proposed to the Board will be presented at the next general meeting with the recommendation of the Board.

Article IV: Dissolution
1. Dissolution shall be proposed, processed, and voted on as for amendments and revisions, Article III.
2. In a case of dissolution of the Society, any funds remaining after payment of all outstanding debts will be donated to one or more organizations, with aims and objectives consonant with those of the Society, to be selected by the Board.

HISTIOCYTE SOCIETY BY-LAWS

The Society shall be governed and guided by the principles set forth in these By-Laws.

ARTICLE I: MEMBERSHIP
Section 1 - Definitions and eligibility. The membership of the Society shall consist of:

A. Ordinary Members
All health care professionals who are active in patient care, education or research in these disorders. Ordinary members pay dues, may participate in all activities of the Society, may hold office, are eligible to vote and receive all communications and publications of the Society, and such special rights and privileges that may be decreed by the Board with the majority-vote consent and approval of the Ordinary members.

B. Honorary Members
Ordinary members who have retired from active involvement in the field and distinguished individuals who, in the view of the Board, will be valued members of the Society. Honorary members enjoy all rights and privileges of Ordinary members but do not pay dues, may not hold office or vote, and will not receive a copy of the Society’s official journal.

C. Emeritus Members
Ordinary members who have retired from active involvement in the field. Emeritus members enjoy all rights and privileges of Ordinary members but do not pay dues, may not hold office or vote, and will not receive a copy of the Society’s official journal. Membership shall be limited to those who function as integral members of a team responsible for work in the field.

Section 2 - Appointment of members and termination of membership
A. A completed application for membership and supporting letter from an Ordinary member is to be sent to the Secretary no less than three (3) months prior to the annual meeting of the Society for consideration by the Board. Applications approved by the Board must be ratified by the membership at the annual meeting.

B. The Executive Board of the Society shall be the sole judge of moral, ethical and professional qualifications required for election to or termination of membership.

C. Applicants will be notified of action taken within six (6) weeks of an annual meeting in which their application has been considered.

D. Honorary members must be proposed to the Board by an Ordinary member and accepted by the Board before ratification by the membership at an annual meeting.

E. Membership shall be canceled on request of the member or on the grounds of: 1) nonpayment of dues for two successive years, 2) failure of the member to attend an annual meeting at least once in three years, or 3) unethical or unprofessional behavior by the member. Cancellation of membership must be approved by the Board.

ARTICLE II: DUES
Section 1
A. The annual dues for Ordinary and Associate members shall be set by the Board and ratified by the General Assembly by a simple majority vote.

B. The annual dues shall be due and payable at the time of the annual meeting or by the date fixed by the Board for the payment thereof.

C. Membership may be canceled for failure to pay dues as set forth in Article I.
ARTICLE III: OFFICERS OF THE SOCIETY

The officers of the Society shall be the president, the immediate past-president, the president-elect, the secretary, and the treasurer. The offices of secretary and treasurer may be held by the same person. All officers must be Ordinary members of the Society and serve without financial compensation. Terms begin and end at the end of the General Assembly of the Society as the final item of business.

A. **President** - Elected for a three-year term, and may be re-elected for one more term, but the second term may not be consecutive.
   1. Presides over annual meetings, is chairperson of the Board, appoints all members of committees not otherwise defined herein, organizes the agendas for Board and annual meetings, co-signs contracts and financial instruments on behalf of the Society, and serves as an ex-officio member of all standing and ad hoc committees of the Society.
   2. Represents the Society in dealing with other organizations and media.
   3. Becomes a member of the Board as the immediate past-president for the year immediately following his/her term of office.
   4. When a member of the Board acts for the then president under the conditions of Article IV.1.B.

B. **President-Elect** - Elected for a three-year term as president. Succeeds to that office at the end of the term of the then-incumbent.
   1. Becomes a member of the Board as the president-elect for the two years prior to assuming the presidency.
   2. When a member of the Board as the past-president acts for the then president under the conditions of Article IV.1.B.
   3. Serves as chairperson of the nominating committee.

C. **Secretary** - Elected for a two-year term with two additional terms permitted by re-election. Is responsible for communication with members and minutes of all meetings, and is ex-officio member of all committees. With the president, co-signs contracts and financial instruments on behalf of the Society. Oversees election of Scientific and Education Committee chairpersons following the annual General Assembly.

D. **Treasurer** - Elected for a two-year term with two additional terms permitted by re-election. Is responsible for all receipts and disbursements of money subject to direction from the Board. Such records as are necessary for auditing purposes must be kept. Recommendations concerning financial matters and the financial status of the Society are reviewed with the Board annually or more often as needed.

ARTICLE IV: THE EXECUTIVE BOARD

Section 1

The executive board (herein referred to as the “Board”) is the governing body responsible for operating the Society. It is composed of the immediate past-president according to Article III.1.A.3., the president-elect according to Article III.1.B.1., the other officers, and two Ordinary members-at-large elected by the membership for a two-year term. All members serve without financial compensation.

A. The Board is required to meet no less than once each year, and it may enroll participation by others, without vote, as needed.

B. If for any reason, as determined by the Board, the president is unable to carry out his/her duties, then the president-elect or the past-president sitting on the Board at that time assumes the duties and responsibilities of the president.

C. Candidates for Board member-at-large shall be ordinary members who have not served on the Board in any capacity for at least two years prior to becoming at-large candidates.

D. A Board member-at-large may serve a second non-consecutive term.

ARTICLE V: FINANCES

Section 1 - Financing of the Society will come through membership fees and from other sources approved by the Board.

Section 2 - Financial records will be audited by an external agency no less than every third year.

Section 3 - An annual budget and accounting of the previous year’s finances are to be presented by the treasurer to the membership at each annual meeting.

Section 4 - Disbursements from the treasury in excess of $1,000US shall require written approval of the Board and must be signed by the treasurer and either the secretary or the president.

ARTICLE VI: COMMITTEES

Section 1

Standing Committees include the Nominating Committee, the Program Committee, the Scientific Committee, and the Education Committee. The president may, at his/her discretion, appoint other committees on an ad hoc basis. The president is responsible for all appointments to committees, with review by and approval of the Board, except as described below.

A. **Nominating Committee** - This committee, composed of the two most immediate past-presidents, and the president-elect (who will act as chairperson), shall be responsible for providing the Board with a slate of officers and candidates for at-large membership on the Board and members of the Scientific and Education Committees, the nominees having established a willingness to serve if elected.
   1. The committee will propose at least one more candidate than the number of vacancies to be filled by election.
   2. This slate must be presented to the Board no later than four (4) months prior to the upcoming relevant General Assembly.
   3. The committee will be responsible for presentation of the slate, as approved by the Board, and for carrying out the election at the relevant General Assembly.
   4. Elections for secretary and/or treasurer and the Board members-at-large shall be conducted at the meeting marking the beginning of the then-incumbents’ last year in office.
   5. Elections for president shall be conducted at the meeting marking the beginning of the last two (2) years in office of the then-incumbent president. The president-elect thereupon becomes a member of the Board according to Article III.B.1.

B. **Program Committee** - The president, secretary, chairperson of the Education Committee and local representative(s) chosen by the Board (members of the Society whose residence is in or near the site of an upcoming annual
meeting) will act as a program committee for the upcoming annual meeting. The president shall act as chairperson. The committee shall be responsible for planning the meeting and for presenting plans to the Board for approval. It will organize and execute the approved program. The committee will also be responsible for planning, organizing and executing other programs in which the Society is officially involved. The committee may recruit, at its discretion, assistance from others who may or may not be members of the Society.

C. Scientific Committee - Vacancies as they occur will be filled by election held at the General Assembly from a slate prepared by the Nominating Committee. Officers of the Society and members of the Nominating Committee are eligible to serve on this committee. Two-year terms will be staggered. A member may serve no more than six (6) consecutive years if re-elected. The committee will select its own chairperson from its membership within ten (10) days of the close of the annual meeting. The chairperson will lead the committee and liaison with the president.

The committee will:
1. Review proposals for research and related activities according to guidelines developed by the Board and make recommendations to the Board.
2. Present the Board with annual reports and plans concerning the Society's research activities.

D. Education, Constitution and By-Laws Committee - Vacancies as they occur will be filled by election held at the General Assembly from a slate prepared by the Nominating Committee. Two-year terms will be staggered. A member may serve no more than six (6) consecutive years. The committee will select its own chairperson from its membership within ten (10) days of the close of the annual meeting. The chairperson will lead the committee and liaison with the president.

The committee will:
1. Suggest one or more topics to the Program Committee for an educational session to be conducted at the time of the General Assembly or such other times as are convenient and appropriate. The topics should be such as to attract not only physicians but also nurses, or psychologists or one of the other groups described in Article II. 4 of the Constitution. The chairperson will lead the committee and liaison with the president.
2. Review abstracts and select those to be presented at the annual meeting.
3. (a) Monitor the Constitution and By-Laws for needed amendments as circumstances dictate, and (b) Be available to the Board for drafting of changes the Board deems advisable.
4. Present the Board with an annual assessment of the Constitution and By-laws.