

ANNUAL REPORT

of the Boyne Research Institute

2007

Boyne Research Institute
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Mission The joint missions of the Boyne Research Institute comprise research and education. Our research mission is to help understand the causes and consequences of diseases during childhood. Our current projects include studies into the causes of birth defects in families, development of Irish young people and their adult achievements (the Drogheda School Leavers Cohort) and the long-term complications of cancer during childhood. Our educational mandate is to provide research experiences for young people from the community, and training for junior scientists.

Objective While retaining our present structure of independence and community base, we are committed to becoming a world-class research institution by expanding partnerships to complement and enhance our capabilities.

Goals for the Next Five Years Development of BRI's capacity to carry out joint epidemiologic-molecular projects with our research partners is a major part of our vision for the next five years. We also aim to expand our student training programmes to include more third-level and post-graduate students from Ireland and from overseas. Expanding our sources of research and training funds is a major prerequisite for these goals.

Website: The website of the Boyne Research Institute carries more information on the research approach, publications and presentations and results of our studies – www.boyneresearch.ie. Reprints are available upon request to admin@boyneresearch.ie.



FROM THE DIRECTOR



Research means constantly facing new challenges, learning new skills, pursuing new ideas. While each year brings its own challenges, 2007 was more challenging than most. Yet, in spite of each of BRI's staff members being stretched in different directions, we learned what we needed to know to get the job done, and came through with a great sense of accomplishment. The scenario was the Pre-Fortification Study, described below.

The challenges had to do with moving away from the tried-and-true methods of telephone interview research into the major challenges of clinical research, that is, obtaining blood samples from our research subjects. This required learning what we needed to know from well-disposed experts in Ireland and in the United States, working through the different technical challenges, including phlebotomy, transport of specimens, sterile technique, and so on. Our staff and volunteers made it all possible, and we are grateful to the HSE (Health Service Executive of the Irish Department of Health) and their staff for facilitating this effort.

Looking forward from this project we are facing into the new era of adding another layer of information to what we already know about Irish families with neural tube defects.

This is the challenge of molecular genetics. With our partners, we are starting into genotyping the blood samples from the Pre-Fortification Study, expecting to have results in 2008.

Funding continues to be a challenge for the Boyne Research Institute. New funding streams will have to be developed in the near future to ensure that our work continues. The Institute, with its joint mission of research and education, is positioned within the knowledge economy. BRI exemplifies the return on investment in the knowledge economy, including enhancing "human capacity in the form of education, training and work experience" (G. Boyle, *Irish Times*, 27 August 2008.) We also add to the sum of "knowledge capital" through our publications, presentations and seminars.

The Boyne Research Institute has been commissioned by a number of national and international bodies to provide support and services for projects as diverse as mental health, breast cancer, childhood cancer and the hazards associated with disposal of human domestic waste. Opportunities to obtain further contract work in the future will be pursued.

I am grateful to the staff, volunteers and board members for their support and good will throughout the year. Support from the community and from friends and foundations in the United States continues to be crucial. I wish to express my appreciation for the vital contributions of everyone to the success of the Boyne Research Institute in 2007

Julie Byrne
Director

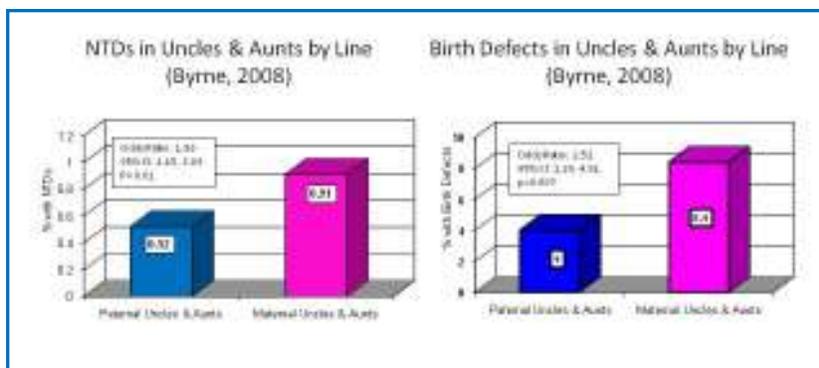


SUMMARY OF RESEARCH RESULTS FOR 2007

1. STUDIES INTO THE GENETIC ORIGINS OF NEURAL TUBE DEFECTS

Overall Objective: To use epidemiologic methods, in this case interviews with family members, to identify patterns of occurrence of birth defects and adverse pregnancy outcomes (miscarriages, stillbirths and preterm deliveries). These are interpreted as markers of underlying genetic susceptibility. Molecular analyses will be carried out in collaboration with research partners. Statistical analysis of molecular characteristics will incorporate epidemiologic characteristics of both families and individual relatives. Ultimately, a diagnostic test may use these factors to determine who is most at risk of having a child with a birth defect, or a pregnancy that ends adversely.

Results:



Results from interviews with uncles and aunts in Irish families with neural tube defects, published in 2008. This slide shows that maternal uncles and aunts are more likely to have neural tube defects (NTDs) and more likely to have birth defects overall than paternal uncles and aunts.

A previously published report describes how some relatives of persons with NTDs are more likely to have pregnancies that ended

adversely, that is, in either a miscarriage, a stillbirth or a preterm delivery (Byrne & Carolan, 2006).

2007 Pre-Fortification Project

Aim: To evaluate the effect of the planned fortification programme in relatives of NTD probands, beginning with a baseline study to determine the level of folate in the blood before fortification.

Objective: This baseline study was intended to determine the levels of blood folate among relatives, and to assess the factors related to serum folate levels. The study was carried out from June to November, 2007; 331 relatives participated and 325 gave a blood sample. The response rate was 49.3%.

Methods: Blood samples from each participant were analysed for blood folate and vitamin B12, and additional samples were stored for future genetic analyses. Participants also completed a demographic and health questionnaire and a dietary questionnaire to measure folate intake.

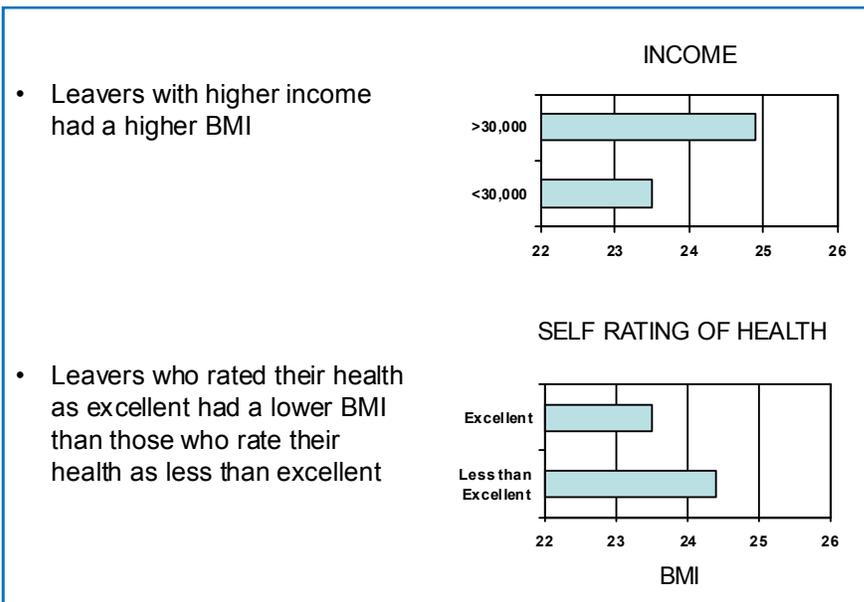
Results: An analysis of data will be completed in 2008 and a paper submitted for publication.

Molecular analysis: BRI has established a collaboration with the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia to evaluate molecular markers.



2. 1993 DROGHEDA SCHOOL LEAVERS COHORT

The Ten-Year Follow-Up of this unique cohort of young people who completed their Leaving Certificate in Drogheda-area schools in 1993 has shown that Leavers gained 10 pounds on average since leaving school.



- Leavers with higher income had a higher BMI
- Leavers who rated their health as excellent had a lower BMI than those who rate their health as less than excellent

To control for different sizes and genders, weight gain was described as Body Mass Index (BMI), a measure that takes height into consideration. Factors related to weight gain were higher current income, and rating health as less than excellent, that is, fair to poor.

See website for more information.

Further follow-up of this cohort is planned.

3. LATE EFFECTS AFTER CHILDHOOD CANCER

Overall Objective: The objective of this project is to initiate and carry out research studies into the long-term consequences of cancer during childhood to survivors and their families in a European context, and with collaborators from the United States.

Background: Survival after childhood cancer approaches 80% in developed countries. The long-term consequences of cancer and its treatment include second cancers, deficits in fertility and cognitive functioning for some, but not all survivors. As treatments evolve and improve, continued follow-up of existing and new cohorts of survivors is needed to provide accurate and timely information for survivors to prevent and remediate where possible the long-term consequences of cancer.

2007 Activities

1. **ELTEC:** (I-BFM Early and Late Toxicity Educational Committee (ELTEC) This is a committee of the International BFM family of clinical trials for leukemia/lymphoma in Europe. In 2007 the group published "The Erice Statement", a compilation of issues related to childhood cancer survival,



developed at a 2006 meeting in Erice, Sicily. Dr. Byrne is an ELTEC member and is heading up two analyses to determine the time when a person who has survived cancer during childhood can be considered cured of their original cancer. Analysis of data from the Childhood Cancer Registry of Piedmont, Italy, was commenced in collaboration with the University of Turin, and a paper planned for publication. The second analysis uses the SEER Cancer Registry of the United States and is being carried out in collaboration with the National Cancer Institute of the National Institutes of Health.

2. **PanCare:** The Boyne Research Institute forms part of a Pan European consortium to establish a Europe-wide study of childhood cancer survivors -- PanCare. A planning meeting was held in Budapest in November 2007.

PUBLICATIONS

1. Linet MS, Byrne J, Willis GB, Wacholder S, Forman MF. Identifying etiologies of pediatric cancers: progress, problems and an exploratory focus group study to understand contextual influences on maternal reporting. Paediatric and Perinatal Epidemiology 21:169-178, 2007.
2. Haupt R, Spinetta JJ, Ban I, Barr RD, Beck JD, Byrne J, Calaminus G, Coenen E, Chesler M, D'Angio GJ, Eiser C, Feldges A, Gibson F, Lackner H, Masera G, Massimo L, Magyarosy E, Otten J, Reaman G, Valsecchi MG, Veerman AJP, Penn A, Thorvildsen A, van den Bos C, Jankovic M, the International Berlin-Frankfurt-Munster Study Group Early and Later Toxicity Educational Committee (I-BFM-SG ELTEC). Long term survivors of childhood cancer: Cure and Care. The Erice Statement. European Journal of Cancer 43(12): 1778-1780, 2007.
3. Byrne J. Birth defects in uncles and aunts from Irish families with neural tube defects. Birth Defects Research Part A: Clinical and Molecular Teratology, In Press, to be published in January 2008.

MEETINGS ATTENDED & PRESENTATIONS

1. ELTEC Annual Meeting, Budapest, Hungary. The Early & Late Toxicities after Childhood Cancer Committee of the International BFM trials group. Dr. Byrne participated in the meeting and presented a talk on "Cure after Childhood Cancer", Semmelweis Medical University, Department of Hematology/Oncology, 29-30 November, 2007.
2. 5th International Neural Tube Defects Conference, September 24-27, 2007, Asilomar Conference Center, Monterey, California, USA. Dr. Byrne's presentation was entitled: "Maternal excess of birth defects among relatives in Irish families with neural tube defects".
3. Dr. Byrne was invited by Prof. Franco Merletti, of the University of Turin, Italy, to give a talk and participate in discussions on an analysis of data concerning "Cure after Childhood Cancer", 7-9 November, 2007.



COLLABORATIONS

For a number of years, the Boyne Research Institute has participated in national and international collaborations, in areas covering developmental problems resulting in birth defects and cancer during childhood. At present, we are involved in collaborative research with research teams in Europe and the United States of America.

- ❖ National Center on Birth Defects & Developmental Disabilities, Centers for Disease Control & Prevention, Atlanta, GA, USA,
- ❖ Division of Cancer Epidemiology & Genetics, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA
- ❖ Cancer Epidemiology Unit, S. Giovanni Hospital & University of Turin, Torino, Italy

OVERSIGHT OF THE BOYNE RESEARCH INSTITUTE, 2007

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We are grateful to those members of our Board of Trustees and the Ethics Board who give freely of their time and energy to help with the mission of the Boyne Research Institute. The Board of Trustees meets quarterly. The Ethics Board meets to review each new project while it is in the planning stages and before the project is implemented. All staff and students are obliged to complete the on-line course in Protection of Human Subjects of the National Institutes of Health (USA).



SUMMER STUDENT PROGRAMME

Objectives The Summer Student Programme aims to provide two or more college-bound students, who have just completed their Leaving Certificate in Drogheda schools, an experience of a research work setting. The programme lasts for 8 weeks and culminates with the students presenting the results their own research project at a Reception at the end of August.

Students In 2007 the two students were Ciara Sheil and Christina Payne, both from Our Lady's College, Greenhills, Drogheda. The titles of their presentations were:

1. Christina Payne: The Effects of Alcohol, Smoking, Drug Usage and Diet on Serum Folate levels among Irish Neural Tube Defect Families, and
2. Ciara Sheil: The Effects of Age, BMI and Parity on Blood Folate Levels.



L to R: Sharon McGinty, BRI nurse-researcher; Ciara Sheil, 2007 Summer Student; Mayor of Drogheda, Anthony Donohoe; Christina Payne, 2007 Summer Student; Julianne Byrne, Director, Boyne Research Institute.

STAFF

In 2007 the Institute retained 3 staff members: Julianne Byrne was assisted by Sharon McGinty, nurse/researcher, and Rebecca Lawler, administrator/researcher.

FUNDING

In 2007, the Boyne Research Institute received grants from the Joseph E. and Marjorie B. Jones Foundation of Washington, DC and from the Drogheda & District Charity Chest. Additional funding was provided by the Friends of the Boyne Research Institute.