



ANNUAL REPORT
of the Boyne Research Institute
2008

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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 our community base, we are committed to becoming a world-class research institute. We aim to achieve this 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 pre-requisite for these goals.

Website The website of the Boyne Research Institute carries more information on the research approach, publications, presentations and results of our studies. Please visit www.boyneresearch.ie. You can also obtain reprints and reports of our studies from admin@boyneresearch.ie.



From the Director

In the past year the Boyne Research Institute made significant progress, establishing new collaborations and realizing the results of research partnerships already established. I am particularly excited about the possibility of obtaining a description of our Irish families with neural tube defects at the molecular level, through a collaboration

established with the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, USA. The results of the analysis are encouraging, and suggest avenues for further research. A second collaboration is commencing with Columbia University (Dr. Salvatore DiMauro), who is planning to screen our families for mutations in mitochondrial DNA (mtDNA). The mechanism of inheritance of conditions arising from mtDNA mutations is similar to what we are seeing in our families with maternal inheritance.

BRI staff in 2008 were concerned with cleaning the data from the pre-fortification study for which data collection occupied the previous year, 2007, and preparing the results for publication and presentation. The major data collection project in 2008 was the Follow-Up Study. The purpose of this project is to re-contact family members, some of whom were last contacted in 1995, and update their family histories. In so doing, we will collect new pregnancy data with which to confirm previous findings.

Our 2008 Summer Student Programme was a great success, enrolling two Leaving Cert students, Ellen Mathews and Patrick Sullivan, and Eimear Kelleher as a summer intern.

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 2008.

Julianne Byrne
Director
Boyne Research Institute



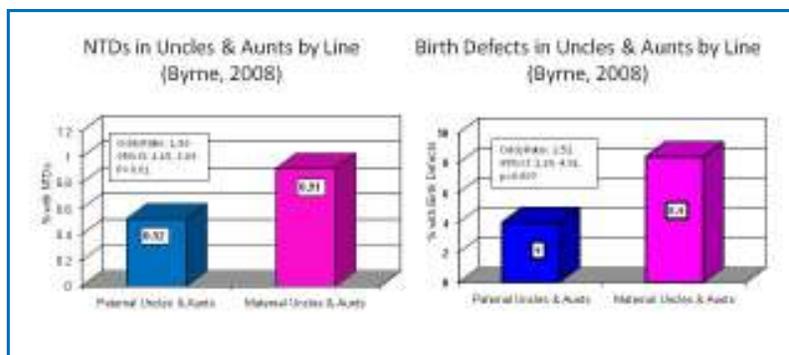
SUMMARY OF RESEARCH RESULTS FOR 2008

1. STUDIES INTO THE GENETIC ORIGINS OF NEURAL TUBE DEFECTS

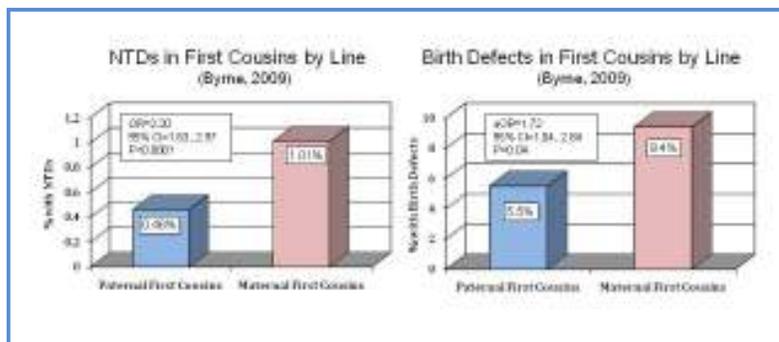
OVERALL OBJECTIVE

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 are being 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.



The pattern of excess rates of neural tube defects, and of birth defects overall continued into the next generation, with first cousins showing the same patterns of inheritance as their parents. A paper describing these results in first cousins was submitted for publication in 2008.

CONCLUSIONS

This pattern of preferential maternal inheritance has been reported in many previous studies for neural tube defects alone, and for the first time by the Boyne Research Institute for birth defects overall. The pattern suggests that some factor is travelling along the maternal line that brings extra risk of birth defects. The factor may be genetic, that is, linked to genes and DNA, or it may be some other alteration in the cell. We are currently investigating these possibilities. The implications for public health are clear: family members, especially those related through the mother, really should be taking folic acid as recommended.



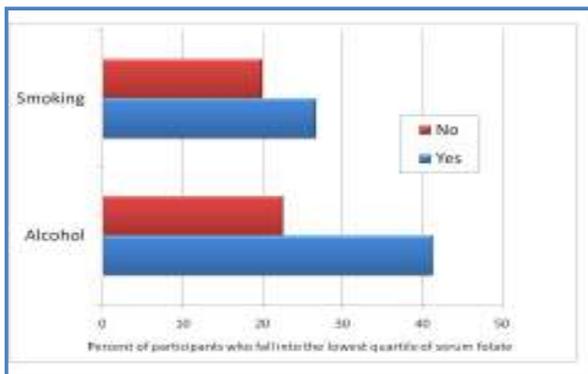
2. 2007 Pre-Fortification Project

BACKGROUND

Close relatives in neural tube defect (NTD) families, including distant maternal relatives, have elevated rates of NTDs and of other birth defects. Folic acid taken as a supplement or in fortified foods raises blood folate levels and prevents most new cases of NTDs. There is little information on blood folate levels among distant relatives. As part of a study intended to evaluate the benefits of fortification of flour with folic acid, we assessed serum folate levels among relatives (probands, siblings, parents, uncles/aunts, first cousins and other relatives) in Irish families with neural tube defects before introduction of the planned fortification programme of the Irish government.

METHODS

Methods: In 2007 325 participating relatives gave a blood sample and completed two short questionnaires concerning lifestyle and dietary folate. A commercial lab measured serum folate levels.

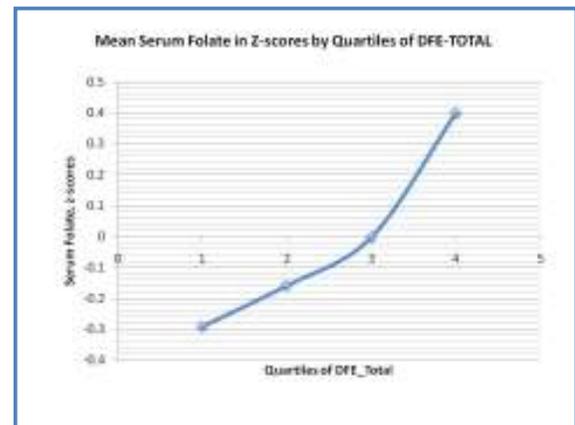


RESULTS, left

A higher percentage of participants who drank heavily, or who smoked, had low levels of serum folate compared to those participants who did not smoke, or who did not drink heavily.

RESULTS, right

On the other hand, intake of folate in all forms (tablets, enriched/fortified food and naturally-occurring in food), measured in four quartiles, from lowest to highest) was a strong indicator of levels of serum folate (see right).



CONCLUSION

Food fortification is an important public health measure that can raise levels of folate in the blood, which in turn has been linked to reductions in the occurrence of neural tube defects.

The Boyne Research Institute strongly urges the Irish government to implement its planned programme of fortification with folic acid to promote the birth of healthy babies.



3. 1993 DROGHEDA SCHOOL LEAVERS COHORT

The Boyne Research Institute has applied for funding in order to carry out an intervention designed to promote healthy living and weight control in this cohort from the Drogheda area.

The 1993 Drogheda School Leavers are now about 31 years of age, just becoming aware of their mortality, and their weight gain may well have continued. In this, they may mirror the general Irish population. Obesity is becoming an Irish problem. About half of Irish people aged 30-44 years are either overweight or obese. Irish children are becoming noticeably overweight. The problem is urgent. Obesity results in diabetes, heart disease, arthritis, cancer and premature death. Our approach to weight control is unusual in that it is to be personalized and community-based. If successful, we and our partners would join in urging the Department of Health and Children to implement our approach in other communities around the country. For more information on the 1993 Drogheda School Leavers please visit <http://www.boyneresearch.ie/schoolleavers.html>.

4. 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 related focused research investigations.

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 and its treatment.

2008 Activities

1. **PanCare:** The Boyne Research Institute forms part of a Pan European consortium to establish a Europe-wide study of childhood cancer survivors called PanCare. A planning meeting was held in Lund, Sweden in March, 2008.
2. **Cure after Childhood Cancer:** An analysis of data from the SEER Cancer Registry of the National Cancer Institute (NIH, USA), in collaboration with Dr. E. Bluhm, Washington Hospital Center.

PUBLICATIONS & ABSTRACTS

1. Byrne J. Birth defects in uncles and aunts from Irish families with neural tube defects. Birth Defects Research Part A: Clinical and Molecular Teratology, 82(1):8-15, January, 2008. PMID: 18044714. <http://www3.interscience.wiley.com/cgi-bin/abstract/117353798/ABSTRACT>
2. Dama E, Maule M, Byrne J, Pastore G, Magnani C, Merletti F. When are survivors of childhood acute lymphoblastic leukemia cured of their original disease? Presented at the Tenth International Conference: Long-Term Complications of Treatment of Children for Childhood and Adolescent Cancer. Niagara-on-the-Lake, Ontario, Canada, 6-7 June 2008.
3. Byrne J, McGinty S, Lawler R. Blood folate levels before fortification in Irish families with neural tube defects. Platform presentation at the Annual Meeting of the Society for Epidemiologic Research, Chicago, IL. June 27th, 2008. Am J Epidemiol 2008;167(Suppl):S145; Abstract No. L11



MEETINGS ATTENDED & PRESENTATIONS

1. PanCare Meeting, Lund, Sweden. Pan-European Cohort Study of Long-Term Survivors of Childhood Cancer. 27-28 March, 2008. Dr. Byrne is a committee member.
2. Tenth International Conference: Long-Term Complications of Treatment of Children for Childhood and Adolescent Cancer. Niagara-on-the-Lake, Ontario, Canada, 6-7 June 2008.
 - Dr. Byrne chaired session on Preservation of Fertility after Treatment
 - Dr. Byrne presented a poster entitled: When are survivors of childhood acute lymphoblastic leukemia cured of their original disease?
3. Annual Meeting of the Society for Epidemiologic Research, 25-27 June, Chicago, IL, USA. Dr. Byrne presented a platform presentation entitled: Blood folate levels before fortification in Irish families with neural tube defects.

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.

- ❖ Dr RJ Berry, National Center on Birth Defects & Developmental Disabilities, Centers for Disease Control & Prevention, Atlanta, GA, USA,
- ❖ Dr. Lars Hjorth, University of Lund, Sweden (chairman, PanCare)
- ❖ Dr. Daniel Green, Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, TN, USA
- ❖ Dr. Salvatore DiMauro, Department of Neurology, Columbia University, New York, NY, USA.
- ❖ Dr. Elizabeth Bluhm, Washington Hospital Center, Washington, DC, USA.

OVERSIGHT OF THE BOYNE RESEARCH INSTITUTE, 2008

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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 advance 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 implementation. All staff and students are expected 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 in August.

STUDENTS

In 2008 the two summer students, Patrick Sullivan and Ellen Mathews, were joined by Eimear Kelleher, who was completing her degree in human nutrition and dietetics from Dublin Institute of Technology. Eimear's internship with the Boyne Research Institute lasted from June to August, 2008.



L to R: Patrick Sullivan, summer student, Julie Byrne, BRI, Mayor of Drogheda, Frank Maher, Mayor of Drogheda, Ellen Mathews, summer student (on left).

L to R: Patrick Sullivan, summer student; Rebecca Lawler, BRI; Sharon McGinty, BRI; Eimear Kelleher, summer intern; Ellen Mathews, summer student (on right).



STAFF

In 2008 the Institute retained 3 staff members: Julianne Byrne was assisted by Sharon McGinty, nurse/researcher, and Rebecca Lawler, administrator/researcher.

FUNDING

In 2008, 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 corporate donors and the Friends of the Boyne Research Institute.