ANNUAL REPORT

Boyne Research Institute

2009

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, 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.

Please visit www.boyneresearch.ie. Reprints and reports of the studies of the Boyne Research Institute can be acquired by emailing admin@boyneresearch.ie.

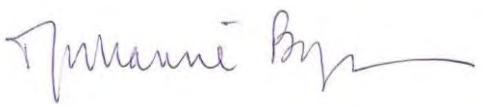
FROM THE DIRECTOR

The year 2009 was a difficult one for the Boyne Research Institute. Economic necessity made it necessary to cut staff, cancel our Summer Student Programme and downsize into smaller premises in the same building. In July, upon completion of the data cleaning of the Follow-Up Study, our research nurse, Sharon McGinty, and our administrator and database expert, Rebecca Lawler, found other part-time employment.

During the year another door opened for the Boyne Research Institute. We continued our involvement in PanCare, a new pan-European network, dedicated to ensure that all European children and adolescents with cancer receive optimal long-term care (page 5). The network is planning a number of grant applications for large-scale studies that would require EU funding. At the end of 2009, the network got word from Brussels that our first stage application was approved; a full grant application will be prepared in early 2010. We look forward to many pan-European projects with this network (www.pancare.eu).

We continued to seek publication of our studies into Irish Families with Neural Tube Defects. Our research results continue to yield new insights, and provide new ideas for continuation (page 4).

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 (Page 6). Much appreciation, too for the staff, volunteers and board members for their support and good will throughout the year. Support from the community and from friends and from foundations in the United States continues to be crucial and greatly appreciated.



Julianne Byrne *Director*

SUMMARY OF RESEARCH RESULTS FOR 2009

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.

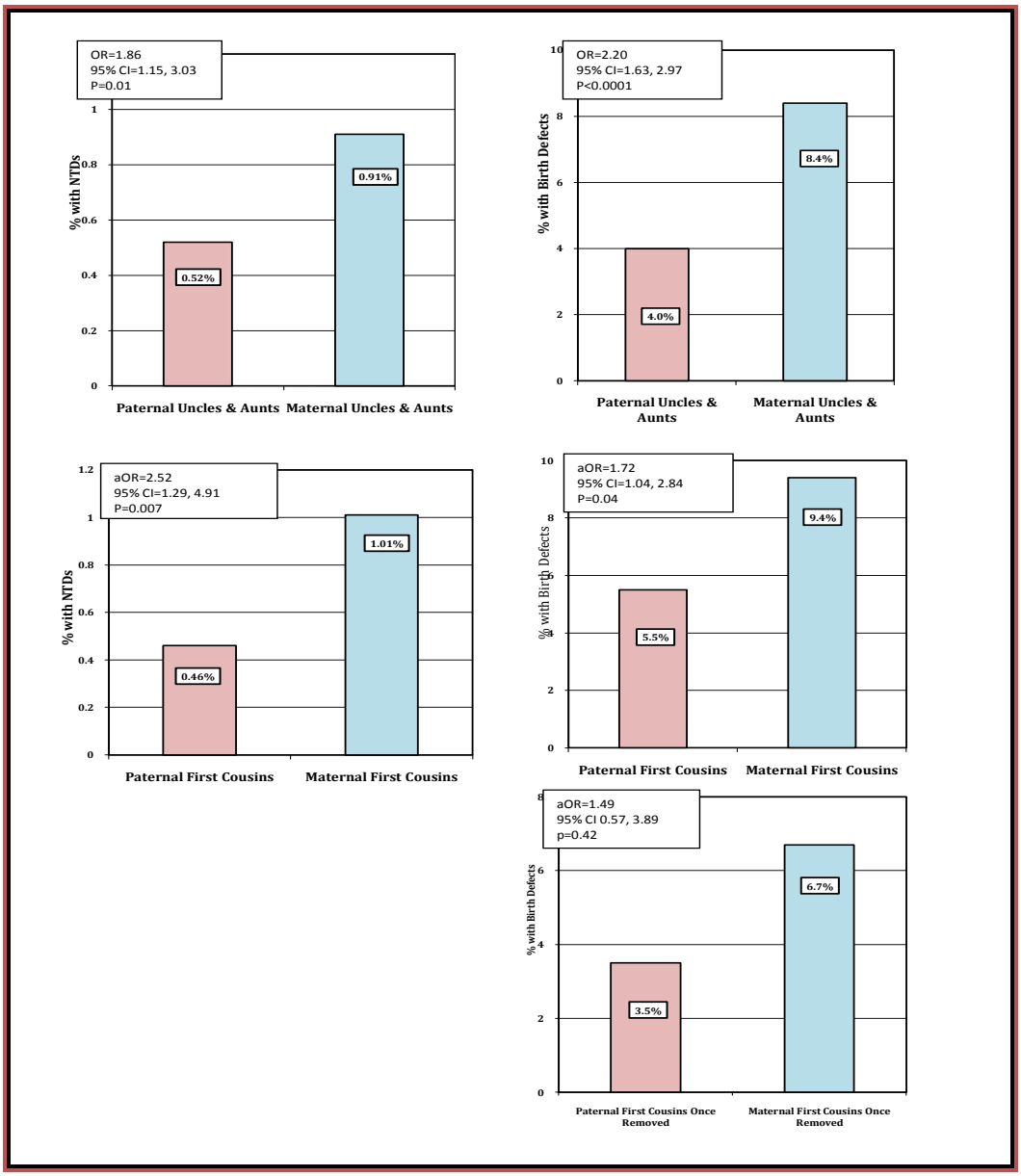


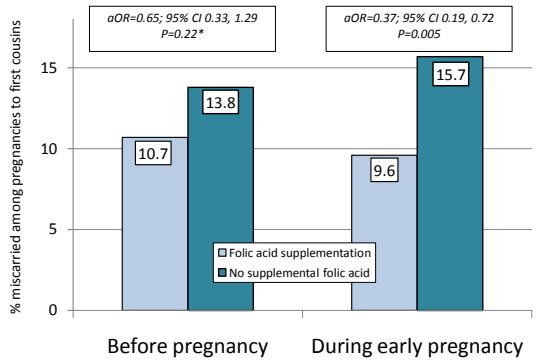
Figure 1. Maternal excess of neural tube defects and birth defects overall in 3 generations of Irish families with neural tube defects. Redrawn from Byrne, Ir J Med Sci, 2010.

a. Excess birth defects among maternal first cousins once removed, as well as among first cousins, and among uncles/aunts.

Neural tube defects (NTDs) and birth defects overall are more likely to occur among maternal compared to paternal relatives in two generations (uncles/aunts and first cousins) of Irish families where an individual has been born with an NTD. The aim of this study was to determine if the matrilineal excess persisted into the third generation. First cousins were interviewed about their pregnancy outcomes and their offsprings' health. Maternal first cousins once removed (FCOR) were more likely to have birth defects than paternal FCOR -- 6.7% vs 3.5% (adjusted odds ratio=1.49, 95% CI 0.57, 3.89). No NTDs occurred. Folic acid supplementation significantly reduced the risk of birth defects (P=0.04). This study demonstrates an excess of birth defects among maternal relatives in three consecutive generations of NTD families, and supports the hypothesis that an underlying mechanism links distant maternal relatives in at least some NTD families.

b. Prevention of miscarriage by supplemental folic acid

Figure 2. Folic acid prevents birth defects overall in Irish families with neural tube defects. Redrawn from Byrne, Ir J Med Sci, 2010



Miscarriages can occur to excess in sibships with neural tube defects (NTDs) and among maternal relatives (compared to paternal) in NTD families. Folic acid prevents most NTDs. Its potential to prevent miscarriages has been controversial. We evaluated the relationship of maternal line and periconceptional folic acid with miscarriage in a cross-sectional study. First cousins in Irish families with NTDs were interviewed about pregnancy outcomes and the health of their offspring. Miscarriages were not more frequent among pregnancies of maternal vs paternal first cousins. Folic acid taken by female first cousins and spouses of male first cousins during early pregnancy significantly reduced the risk of miscarriage among their pregnancies from 15.7% to 9.6%, for an adjusted odds ratio of 0.37 (95% confidence interval 0.19, 0.72, p=0.005). In this study folic acid taken during pregnancy was associated with a reduction of approximately 60% in miscarriages. Miscarriages are common – one in every eight pregnancies in this study. If incorporated into pre-pregnancy counseling these results could have significant public health impact.

c. Follow-Up Study of Relatives in Irish Families with Neural Tube Defects

Since some relatives had not been contacted since 1995, we designed a Follow-Up Study of relatives, with the objective of determining a) the proportion of pregnancies that ended in miscarriage and the proportion with birth defects, and b) if the pregnancies that were supplemented with folic acid were more or less likely to end in miscarriage, or in a child with a birth defect, than pregnancies that were not supplemented.

Relatives were eligible if they were able to give informed consent, were blood relatives, were between the ages of 18 and 45, and were any type of relative (proband, father, mother, uncle, aunt, first cousin, first cousin once removed, sibling, niece or nephew. The number of relatives who were known to be eligible was 633. Between May 2008 and June 2009, 494 relatives were interviewed, for a response rate of 78%.

Relevant pregnancy information from this study were incorporated into the analysis of data concerning birth defects in first cousins and also, into the analysis of data concerning miscarriages and folic acid.

2. Late effects after childhood cancer

a. 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.

b. 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.

c. 2009 Activities

i. Collaboration with CCSS: The Childhood Cancer Survivors Study (CCSS) is a US study of a large cohort of long-term survivors of childhood and adolescent cancer (http://ccss.stjude.org/). The Boyne Research Institute collaborated with scientists from St. Jude's Children's Research Hospital in Memphis, Tennessee, in analyses of fertility among male and female survivors of childhood cancer using CCSS data.

ii. PanCare: The Boyne Research Institute forms part of a Pan European consortium to establish a Europe-wide study of childhood cancer survivors called PanCare (www.pancare.eu). A new study, called PanCareSurFup for PanCare Childhood and Adolescent Cancer Survivor Care and Follow-Up Studies, was prepared and submitted as a first-stage application to the 7th Framework Programme of the EU (7FP). Our project consists of a bundle of tightly-linked studies into the risk of late mortality, second cancers and cardiac disease among childhood cancer survivors, and includes a project on establishment of guidelines for long-term follow-up, and dissemination of the research results. The first stage was approved, and a full application is to be prepared for submission in early 2010.

PUBLICATIONS & ABSTRACTS

1. Green DM, Kawashima T, Stovall M, Leisenring W, Sklar CA, Mertens AC, Donaldson SS, Byrne J, Robison LL. Fertility of female survivors of childhood cancer. A report from the Childhood Cancer Survivor study. Journal of Clinical Oncology, 2009 Jun 1;27(16):2677-85. Epub 2009 Apr 13. PMID: 19364965. http://www.ncbi.nlm.nih.gov/pubmed/19364965?ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum
2. Hjorth J, Haupt R, Skinner R, Debling D, Kremer L, de Vathaire F, Hawkins, M, Garwicz S, Frey E, Byrne J, et al. PanCare – A new kid on the European childhood cancer survivor block. Platform presentation at the ESLCCC2009 (European Symposium on Late Complications after Childhood Cancer), Edinburgh, UK, 29-30 November 2009.
3. Frey E, Levitt GA, Kremer LC, Byrne J, Skinner R. European survey of transition programmes for adult long-term survivors of childhood and adolescent cancer. Poster presentation at the ESLCCC2009 (European Symposium on Late Complications after Childhood Cancer), Edinburgh, UK, 29-30 November 2009.

4. Michel G, von der Weid N, Byrne J, Debling D, Essig S, Hjorth L, Skinner L, Haupt R, Kremer L, Frey E, Bardi E, Kuehni E. Follow-up care after childhood cancer in Europe: A pilot study. Poster presentation at the ESLCCC2009 (European Symposium on Late Complications after Childhood Cancer), Edinburgh, UK, 29-30 November 2009.

MEETINGS ATTENDED & PRESENTATIONS

1. J. Byrne: Sixth International Neural Tube Defects conference; The Essex, Burlington, Vermont, USA, Sept 12-15, 2009. Presentation: Protective effect of periconceptional folic acid against birth defects overall and miscarriages.

2. J. Byrne: 4th PanCARE Meeting, 26th-28th October, 2009-07-08, Newcastle upon Tyne, UK

OVERSIGHT OF THE BOYNE RESEARCH INSTITUTE, 2009

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