The Founding of the Institute of Brain Chemistry and Human Nutrition 1989

The beginning

The Institute of Brain Chemistry and Human Nutrition (IBCHN) was formed in 1989 as an independent research institute with the objective of applying seminal discoveries made by Professor Michael Crawford and his team in the 1970s of a requirement for the ω3 docosahexaenoic acid for brain growth and function to human early development [1], [2],[3]. The primary aim was to test for a relationship between maternal and fetal nutrition and risk of neurodevelopmental disorder. The reason at that time for was that or prior research had pointed to the paramount importance of DHA and arachidonic acid in brain development joined with the almost total absence of applying this knowledge to food policy or education. It was evident to us that the brain is what makes us different from monkeys and apes. Moreover brain disorders were commonest in those born very preterm and at very low birthweights. Hence the formation of the Institute was motivated by the need to address this issue by translating the knowledge to human pregnancies. Hence the first challenge was to study maternal nutrition and low birthweight.

Steering committee 1989-1990

It was founded following extensive peer review and a council comprised of Lord Rea of Eskdale, Sir Michael Marmot, Professors Gerry Shaper and Kate Costeloe, Dr. Robert Lister (current chair), Margaret Wynn, Ian Dawson-Shepherd (founder of Scope), Michael Pirkis, Major Christopher Robinson (current chair of the Mother and Child Foundation) and chaired by Professor Cedric Hassall FRS. The Council met on six occasions to formalise the identity, mission, structure, £1 million funding and research direction.

Aim

The primary aim was to address adverse maternal nutrition[4] and health leading to unfavourable fetal development because

(i) seventy percent of the energy delivered from the mother is devoted to fetal brain growth

(ii) the brain is a lipid (fat) rich organ with precise lipid requirements[5],[6]. These were delineated by the research group but were nowhere to be seen in practice or in infant feeding[7].

(iii) The nutrition of the mother was not thought to influence the fetus, but IBCHN studies showed that it was.[8],[9],[10],[11].

(iv) (iv) The cost of neurodevelopmental disorder[12],[13] was and is disproportionately high because of its lifelong impact. Mental ill-health has now overtaken all other burdens of ill-health. Further escalation of mental ill-health is unacceptable and a threat to civil society.

Research in the East-end of London:

The IBCHN as the research arm of the Mother and Child Foundation was self funded. It was provided with laboratory facilities by Dr. Ken Grant, then in charge of Hackney Medical Services . Originally the work was done at Hackney Hospital. Due to rebuilding works it then moved to the Queen Elizabeth Hospital for Children. The service supported the work because Hackney and Tower Hamlets had the highest incidence of babies being born small for gestational age and very preterm. Much of the early work was done in collaboration with Professor Kate Costeloe at the Special Care Baby Unit of Homerton Hospital to test for an involvement of maternal and fetal nutrition in pregnancy outcomes, especially in terms of very preterm births. Wendy Doyle ran the maternal nutrition studies from the Mother and BABY Clinic in Well Street

near the Homerton Hospital. The MBC was made possible by a generous donation from the later Dr. Anne Gibson.

The Institute was formed with a readymade international reputation having worked as a WHO collaborating laboratory for studies on human milk lipids[14] and with the Chinese Academies of Medical Science and of Preventive Medicine for the 65 County study of nutrition and chronic diseases in China[15]. Almost immediately after formation it contributed to the Nicholas Winterton MP's, Parliamentary Select Committee on Maternity Services in 1990 and carried out a survey for WHO and the Department of Health in Indonesia on the high incidence of mental retardation and anemia in pregnancy in 1992.

The research was done at the Hayward Research Building of the Queen Elizabeth Hospital for Children in Hackney. In 1996 it was invited to join the University of North London as an independent research institute. The late Maggie Sanderson at North London, saw the synergy with her teaching of State Registered Dieticians and the work of the IBCHN. Tragically, the University made false claims over false claims on student numbers for money and now has to pay back £36.5 million to the Higher Education Funding Council. The consequent cuts led to situation for IBCHN at the University to be untenable. Professor Crawford has been appointed as a visiting Professor to Imperial College at the Division of Reproductive Biology at Chelsea and Westminster Hospital Campus where the IBCHN can be re-located.

The Institute recently won an EU and collaborates with the University of Bergen, The Weizmann Institute, the United States Department of Agriculture, the University Medical School of the Sudan, the Government of Oman and the Health Protection Agency in China. Its Randomised Clinical Trial of supplementing women from early in pregnancy has confirmed previous findings by reducing the number of babies born small for gestational age 2.3 fold. It is now clear from the work that maternal nutrition specific to brain development in pregnancy if not before, is a major determinant of the rise in mental ill-health which has overtaken all other burdens of ill health . The IBCHN is one of the few institutes with the knowledge to address the rise in mental ill health.

New Aim of the Institute at Imperial College:

The cost of mental ill health in the UK is now greater than that of heart disease and cancer combined. The aim is to disseminate existing knowledge and provide the necessary new science to arrest and reverse the brain stunting and rise in mental ill health. To do this it will be necessary to re-create the IBCHN at Imperial College where the opportunities and support for research are world class. It will be necessary to raise money to transfer the staff and re-create the Institute with new staff to address the rise in brain disorders. In particular the aim is to bring in young people and look for a new leader for when Professor Crawford retires to continue to develop the new paradigm of brain research, provide advice on policy and action on the climbing morbidity from brain disorders and mental ill health.

Current Research Activities:

The research is ably coordinated by Dr Yiqun Wang who has worked with the Institute for 12 yearsa,.

- The Institute completed a phase II clinical trial of micronutrient supplementation in the East end of London which significantly reduced the number of small for gestational age babies by almost a half. A study of 450 mothers[16] with positive benefits for pregnancy outcomes and prevention of babies being born small for gestational age needs urgently to be repeated in a larger, multi-centre trial. This trial needs to be focussed more strongly on brain development with Magnetic Resonance Imaging on brain development to provide robust quantitative data on brain development. Being born small for gestational age is the strongest risk factor for poor school achievement, behavioural pathology and chronic ill health such as heart disease and stroke.

- We then wish to apply the omega 3 index, a marker of the status of the most important signalling molecule in the brain, as an early indicator risk of adverse neurodevelopment. This wil be a first step to nation wide prevention of developmental brain disorder and mental ill health.
- Studies on school children's nutrition, especially the girls in puberty demonstrate the real need for education on nutrition and health in the schools. Nearly one third of the girls we studied were iron deficient as measured by their blood status. It will not be long before they will become mothers[17].
- A clinical trial on omega 3 supplementation in pregnancy for women who become diabetic in the pregnancy and for those who are diabetic. We are testing the possibility that omega 3 supplements will protect fetal brain development from the adverse consequences and will protect the mothers from the diabetes. This is at Newham General Hospital and Chelsea and Westminster Hospital. The results of the trial will appear in 2012 although much valuable information is being gathered and published as it appears. However data is already available from those with pre-eclampsia.[18]
- Research on the high risk of diabetes and dementia in Down's syndrome and on children with ADHD are currently underway in collaboration with the Institute of Psychiatry[19] and in Warsaw.
- A phase II trial on stroke in children with sickle cell disease has just been completed successfully which we hope will lead to a cheap treatment to control the severely painful crises and prevent the strokes in children which damage the brain and can substantially reduce their IQ[20].
- A study of maternal nutrition and iodine deficiency disease which is common in the Sudan[21]. This study is combined with research on maternal nutrition through the study of breast milk showing clear evidence of omega 3 deficiency co-existing with iodine deficiency.[22] Ths implication of a co-esisting iodine and omega 3 deficiency has global significance. There are 2 billion people known to be at risk oif iodine deficiency and consequent brain stunting in the children.
- Research on why DHA and only DHA has been used in the receptor and signalling structures of vision and the brain for the whole time period of animal evolution is underway with the US Department of Agriculture. No other molecule has replaced it in vision and the brain over 600 million years of evolution[23]. This direction has developed into an explanation for the irreplaceable use of DHA in neural signalling.
- The Institute was also engaged in basic research with Bergen University and the Weizmann Institute on neurogenesis and brain development to enhance our understanding of how DHA in particular[24] promotes brain growth and development and function.
- Following on the work in the East end (see above) a randomised trial of essential fatty acids in pregnancy was been completed in 2015. Some 6 papers will result on the predictive value of faty acids at the first ante-natal recruitment for preterm delivery, birthweight and head circumference, the effect of the supplement during the pregnancy, impact on gut flora, maternal mental health and on imaging of the brain at or around the time of birth.

The future involves expanding the work on maternal nutrition in London and being born small for gestational age which is the strongest risk factor for poor school ability and chronic ill health and indeed the cycle of poverty. We will also develop the work in Africa where malnutrition of the mother and the child under two years of age is leading to loss of full abilities, chronic ill health and again the cycle of deprivation. A similar project will be discussed in China in October.

Having successfully held a conference on DHA and the brain at the Royal Society of Medicine follow up initiatives are being taken for Melbourne in November and Minneapolis in 2011. Action needs to be taken to prevent a continued increase in mental ill health and brain disorders which up to now have been sideline. Professor Crawford was raporteur for the 1978 joint FAO-WHO consultation on role of dietary fats in human nutrition and was invited as an expert to the 1994 and 2008-2010 WHO-FAO consultations.[25]

Whilst continuing to develop knowledge on the causes of brain disorders the immediate aim is to raise awareness of the supreme importance of the health and nutrition of the mother and child, the need for

education and action to prevent the rise of brain disorders which have now overtaken all other burdens of ill health. In 2004 in the 25 EU the cost was €386 billion and in 2007 in the UK alone it was £77 billion. It rose to €789 billion in the EU in 2010 and £105 billion in the UK that same year. The Wellcome Trust Web site estimated the cost in 2013 at £113 billion. The cause is almost certainly the loss of marine foods in the wake of the increase in intensively produced land based foods. The arrest of this rise has to the most urgent priority in action and research.

Future work and funding requirements:

Whilst the Institute is core funded by the Mother and Child Foundation there is an urgent need to develop :

- Phase II trial on micronutrient supplementation in pregnancy
- and on sickle cell disease in Oman
- Research on DHA and on neurogenesis,
- Cerebral Palsy and allied neurodevelopmental disorders.
- Down's syndrome as a prime example where application of the existing evidence base on risk of obesity, diabetes, heart disease and dementia can be applied now to the growing children. Whilst at the same time, research to better understand the distortions made by the extra copy of chromosome 21 could lead to a better understanding of this cluster of lipid related disorders.
- The application of the new understanding of the significance of brain specific nutrients to inappropriate maternal and infant nutrition has global implications to malnutrition in developing countries and the inner city regions of developed countries.
- The co-existence of omega 3 deficiency with iodine deficiency is affects 2 billion people.
- A study f 50,000 pregnancies to delineate the nutritional relationships with severe neurodevelopmental disorders as in cerebral palsy, epilepsy, autism and behavioural pathology.

The application of the knowledge gained and the need to tackle the rise in brain disorders predicted by the researchers of IBCHN in 1972 is the most urgent. With brain disorders have overtaken all other burdens of ill health in Europe and predicted to be no 2 in the world wide burden of ill health by 2020[26], we are facing what is perhaps the greatest threat to humanity in the full meaning of the word.

Tackling this issue again requires the translation of existing knowledge into education, health, fiscal and food system policies where a new paradigm is needed. Last century the food system was based on protein and calories. There was no consideration of the nutrition of the brain. Different set of nutrients are required for the growth, development and function of the body ad of the brain. This truth can be seen in the large fast growing land mammals which develop a large body and little brain as in the great apes and other large mammals like the rhinoceros which reaches a one ton body weight after 4 years of growth but only has 350g brain. The threat of the rise in brain disorders of which mental ill health is the most prominent, needs a multi-disciplinary approach by Government and research prioritised to advance our knowledge on prevention.

The Institute was recognised for its pioneering work in May 2010 at a two day meeting on DHA at the Royal Society of Medicine where it was entered into the Society's Hall of Fame. It hosted a month long exhibition at the Society which presented the evidence and spelt out the gravity of the situation as it impacts on the threat to the sustainability of the human brain. A new dimension in funding is required to ensure the science is fully disseminated to the decision making political system and that is continues to develop the needed new knowledge whilst at the same time implementing actions and policies to help prevent the escalation of mental ill health. The brain is affected in a multi-generational manner. Deficiency of DHA is not like vitamin C deficiency which can be corrected in a few days. Tackling the rise we are now seeing of brain disorders is a long term, multi-disciplinary project involving many dimensions in research, food, agriculture, fisheries,

health and education. It is the most urgent priority and we would say is a more urgent and serious issue then global warming.

Most recently (2015) he Director received the Chevreul Medal in Paris for identifying he role of DHA in the brain and the Order of the Rising Sin for contribution to culture and Science.

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