



**TRUSTEES REPORT
EXTRACTS - YEAR TO 30 SEPTEMBER 2002**

Significant events

The following detail set out in paragraphs 1 and 2 below is a report of the work of Dr Susan Hall who was awarded grants from the Foundation over the period under review. The grant holder is Professor David Hall of the School of Health and Related Research, Sheffield University.

1. Epidemiological surveillance of Reye's Syndrome (RS) and related scientific matters

(a) Cases of RS Reported

As noted in last year's report, surveillance of RS via the British Paediatric Surveillance Unit ceased in April 2001. However, the arrangements with The Office of National Statistics and The General Register Offices of Northern Ireland and Scotland continued to be maintained throughout the year. Under these, the Offices sent Dr Hall copies of all death entries where RS was mentioned as a cause of death, whatever the age of the subject.

In the year ended 30 September 2002, no RS deaths were reported from Scotland; there were no RS deaths in Northern Ireland in 2001 but data for 2002 are still awaited; for England there were three deaths - a 35 year old man in December 2001, a 13 year old girl in April 2002 and a one year old boy in May 2002. Only the second case had classical RS and she had been given aspirin. One further death was notified during the year, although the child, a 13 year old boy, had died in 2000.

This was an atypical case, being a sudden unexpected death, and there was no report of aspirin having been given.

There are three other possible mechanisms by which RS continues to be monitored: the most important, because it is permanent, is the 'yellow card' adverse drug reaction (ADR) voluntary reporting scheme run by The Medicines Control Agency (MCA - now called The Medicines & Health Care Products Regulatory Agency MHPRA). As RS is an adverse reaction to aspirin, all aspirin associated cases should be reported. Dr Hall informed the MCA about the 13 year old girl mentioned above. The case had not been notified at the time, but the report was subsequently Validated by the MCA via the clinician and the pathologists involved and was Officially entered into the ADR system.

There are two studies conducted via the British Paediatric Surveillance Unit which might ascertain cases of RS. Dr Hall is not directly involved with them, but has asked to be informed if this occurs. They are surveillance schemes for Suspected Fatal Adverse Drug reactions in Children, which runs between June 2002 and June 2003, lead investigator Professor Terence Stephenson, Queens Medical Centre, Nottingham; and Severe Complications of Varicella, which runs for one year from Autumn 2002, lead investigator Dr Claire Bramley, Scottish Centre for Infection and Environmental Health, Glasgow.



(b) Work with the MCA/MHPRA and Associated Work arising from representations made by the European Aspirin Foundation (EAF)

It was noted in the previous report that, towards the end of 2001, the Committee on Safety of Medicines had considered reversing its earlier decision not to increase the age limit on the aspirin warning. This was at least in part because of representations made by Dr Hall based on results from the Reye's Syndrome Surveillance Scheme. A new warning was subsequently announced in April 2002 which stated 'do not give to children under 12 unless medically indicated and avoid in children aged up to and including 15 if feverish'. There was modest media coverage but no major public information campaign or indication as to when product labelling would change.

In October 2001, presumably at a time when the CSM/MCA was discussing its proposed new labelling with industry, Dr Hall was approached by the chairman of the Liver Steering Group (LSG) of the British Society for Paediatric Gastroenterology, Hepatology and Nutrition, for advice on how to respond to representations recently made to its members by the EAF. The EAF was seeking help to 'resist pressure from the MCA to agree to a voluntary ban on aspirin use in teenagers'. Dr Hall prepared a briefing paper to assist the LSG chairman in his discussions with his members as to how to respond to the EAF. In the end, the Society decided not to assist the EAF with an opinion on this issue.

In May 2002 Dr Hall was asked by the MCA to comment on the proposed new warning after she had written to ask when there was to be a publicity campaign and changes to labelling. She pointed out that the plan to delay the campaign until the start of the following influenza season could result in the occurrence of preventable cases of RS in teenagers in the ensuing 6 months or so. Unfortunately the response was that there was concern that an 'immediate' public campaign would cause alarm and have a negative impact on the use of aspirin for important therapeutic indications such as cardiovascular prophylaxis. The MCA considered that alerting medical professionals was sufficient at that time. Dr Hall registered her concern at this approach. {In October 2002, the CSM decided that the April warning was too complex and modified it to 'do not give to children under 16 years unless on the advice of a doctor'}.

(c) Advisory Scientific and Medical Support for the National Reye's Syndrome Foundation

Over the period under review, Dr Hall has advised the Honorary Administrator – Mr. G. Denney – on a number of issues arising from correspondence received by him. These included a further review, following referees' responses, of a grant application from the School of Biomedical Sciences, Queens Medical College (QMC) Nottingham, to undertake laboratory studies into the causation of RS. There was also a new grant application from the Division of Child Health at QMC, Nottingham, submitted in July 2002. It had been stimulated by the Workshop (see below) and its purpose was to develop a guideline for the diagnosis, investigation, and management of acute encephalopathy, including RS and metabolic disorders presenting as Reye-like illness in childhood. The application was refereed by 8 reviewers including Dr Hall and the Foundation's Medical and Scientific Advisory Board.

In September 2002 the Foundation was approached by the EAF with a further request for a meeting to revisit the evidence linking aspirin and RS (they had earlier made such a request in April 2000 - see annual report 1999/2000). The EAF



(c) Advisory Scientific Advisory and Medical Support for the National Reye's Syndrome Foundation (continued)

considered that some recent publications justified this and also enclosed material devised by them for a public information campaign about the new age limit on the warning (see 1b above). Dr Hall reviewed all the evidence as well as the original request and advised the NRSF that there was no case for such a meeting. She advised the NRSF to express concern about some of the content of the EAF material. The correspondence was copied to the MCA, who also expressed concern about this material.

Other support includes responses to medical queries from members of the public and assistance with an update of the Foundation's leaflets.

2. Professional education – Workshop on RS and Reye-like inherited metabolic disorders

The background and preliminary plans for this Workshop are outlined in previous Annual Reports, 1999/2000 and 2000/2001. In summary, its purpose was to bring together epidemiological, clinical, biochemical and pathologist experts in the field of RS and RS-like illness to discuss issues of diagnosis and management which would lead to development of an educational package or formal clinical guideline for front line accident and emergency doctors, paediatricians and intensivists.

The Workshop was residential and was held over one and a half days in March 2002 at a College of Further Education near Doncaster. There were 28 participants including 2 moderators (Dr Roddy McFaul and Professor David Hall, the then President of the Royal College of Paediatrics and Child Health). Among the participants were - paediatricians specialising in inherited metabolic disorders (IMDs), IMD specialist nurses, paediatric neurologists, paediatric hepatologists, paediatric A & E specialists, a paediatric intensivist, clinical chemists, paediatric pathologists, general paediatricians and a guideline methodologist. There were two parent representatives - one from the National Reye's Syndrome Foundation (Mr G Denney), the other from CLIMB (Mrs L Greene).

In November 2001, a briefing document was sent to Workshop participants which included a framework of detailed questions which broke down the main issues into a series of small steps in question form. Twenty six participants were invited to address specific questions related to their area of expertise. They were asked to submit a short paper with their responses supported by published evidence wherever possible. These papers were submitted in advance and circulated prior to the Workshop so that, on the day, only a brief oral presentation was required and most of the time could be spent in round table discussion.

The main subject headings of the sessions were - "what is the evidence that we have a problem?; clinical diagnosis; laboratory diagnosis; autopsy diagnosis; management; obstacles to achieving best practice; dissemination and implementation of educational packages/guidelines".

The entire meeting was professionally recorded and the transcript typed. The organisation of the meeting was undertaken by Dr Hall supported by a small Steering Group. The Workshop was fully funded by the National Reye's Syndrome Foundation. Participants considered that it had been most successful. One of the



2. Professional education – Workshop on RS and Reye-like inherited metabolic disorders (continued)

most important outcomes was the stimulation of a highly respected and experienced group at Nottingham University to submit a grant application to the Foundation for development of a formal guideline (see above). This was unlikely to have happened in the absence of the Workshop.

Shortly after the Workshop, Professor David Hall and Dr Susan Hall submitted a grant application to the National Reye's Syndrome Foundation for a 1 year extension to their previous grant. This was to enable Dr Hall to:

- i) Prepare a report on the proceedings of the Workshop based on the edited transcript. It was proposed that this should be made available eventually on a CD and on the Reye's Syndrome Foundation website. The CD would be publicised via the website and the Royal College of Paediatrics and Child Health and was hoped to be subject of an annotation to be submitted to the Archives of Disease in Childhood by the Workshop Steering Group. It would also be made available to the Nottingham researchers preparing the guideline (see above).
- ii) Prepare a report for publication, on 20 years of epidemiological surveillance of RS in the UK and Ireland.
- iii) Implement permanent storage of the RS database.

After external refereeing, the grant was awarded in August 2002 and work on the proceedings is currently (May 2003) in progress.

Submitted by
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