

## Handout to parent(s)/guardian

Through parents such as you, Doctors at the Royal Free Hospital School of Medicine, have been alerted to the possible existence of a new disease: this comprises the development of autistic features in children who were apparently developing normally, and intestinal symptoms such as pain, diarrhoea and failure to thrive. The problem has been associated anecdotally, but consistently, with measles or measles/rubella vaccination. We, at the Royal Free, have now looked into the background medical and scientific literature concerning this problem, and have formulated the hypothesis that in certain (perhaps genetically susceptible) children, live-virus vaccines may produce longterm inflammation of the intestine and failure to absorb, in particular, vitamin B12. In the developing brain this vitamin is vital, and young children are very sensitive to B12 deficiencies. Such deficiencies may lead to failure of normal brain development and regression of behavior similar to that you have possibly observed in your own child.

We would like to carry out a series of tests which, we believe, will help us to establish the features of this possible disease. Our aim is to characterise the problem so that, for the future, we may be able to treat affected children and improve their wellbeing.

You and your child will be admitted to Malcolm Ward at the Royal Free on a Sunday, and will stay for one week. On Sunday you will be seen, interviewed, and your child examined, by a Paediatric doctor. During this interview you will be asked about any allergies or drug reactions that your child might have had, so that these contacts can be avoided during your child's admission. On Sunday evening your child will receive a laxative that prepares the intestine for examination the following day. Your child will have water only from midnight on Sunday until Monday lunchtime. On Monday morning you will both go to the Endoscopy Suite on the 10th floor where, after an intravenous sedative injection, a blood sample will be taken and your child will have a telescopic examination (ileocolonoscopy) of the large bowel (colon) and the last part of the small bowel (ileum) and the upper digestive tract (upper endoscopy). These procedures are usually tolerated well by children, lasting about half an hour. If your child becomes distressed or the procedure proves to be too difficult with sedation alone, it will be performed under a light general anaesthetic. During the procedure, small pieces of tissue will be taken from the bowel for analysis. This is a vital part of the procedure, and is entirely painless.

Following the ileocolonoscopy and still under sedation, your child will undergo a lumbar puncture on Malcolm Ward. This procedure involves the introduction of a needle into the space around the nerves in the lower back in order to obtain a sample of the fluid surrounding these nerves. This fluid will be sent for examination of possible responses to the measles and rubella viruses and evidence of inflammation in the brain. The lumbar puncture is performed after the injection of a local anaesthetic into the skin of the lower back. The local anaesthetic itself produces a mild brief stinging sensation. Thereafter, the procedure is entirely painless.

Over the course of the next 4 days your child, accompanied by you throughout, will have a brain scan (MRI scan) that will also be performed under sedation. The scan lasts about 30 minutes and is both safe and painless. An electroencephalogram (EEG) will be performed; this procedure involves measuring brain-wave activity through electrodes placed on the head. Once again it is painless. Towards the end of the week your child will have a test to measure the ability of the intestine to absorb vitamin B12. This is a routine procedure which involves taking a very small quantity of radioactive material mixed in scrambled egg. Over the next 24 hours the urine is collected into a special container, and analysed to measure the

amount of vitamin B12 that has been absorbed.

In addition, it may be necessary to perform a special X-ray of your child's intestine. This is called a *barium follow-through* and involves taking a harmless milky-coloured liquid which is then photographed as it passes through the intestine. This examination will be performed only if the ileocolonoscopy suggests there is some abnormality of the small intestine.

Finally, you will be interviewed with your child by both a Consultant Neurologist and a Consultant Physician from the Department of Child and Adolescent Psychiatry. These experts will seek to clearly identify the features of your child's development/behaviour problem.

On Friday your child will be discharged, to be followed-up in the outpatients. The tissue and blood samples will be analysed, and the results - reported to you, as far as they are complete, at the clinic appointment. Any further recommendations regarding treatment and follow-up will be made at this stage.

15. DATE OF SUBMISSION: 16th September 1996

SIGNATURE OF INVESTIGATOR: 

Please type NAME and DEPARTMENT in CAPITALS (and/or address with telephone number).

NAME: A J WAKEFIELD

DEPARTMENT: ACADEMIC DEPARTMENT OF MEDICINE

16. PLEASE REPORT WHEN THE STUDY IS COMPLETED. FOR ETHICAL COMMITTEE ADMINISTRATION USE ONLY

16. ETHICAL PRACTICES SUB-COMMITTEE DECISION

Submission Number .....

(a) Consideration deferred for the following reasons:-

Signed ..... Chairman

Meeting No. .... Date .....

**CONSENT FORM**

Name of Child/ward.....

I have read and understood the aims and nature of this study and have discussed, in detail, the implications of the study with the Doctors concerned. I hereby agree to let my child/ward ..... take part in the study. I understand that I can withdraw my child/ward from the study at any stage without prejudicing his/her management or treatment in any way.

.....  
Signature of Parent/Guardian giving consent

.....  
Print name

Date: .....

.....  
Signature of Doctor obtaining consent

Date:.....

.....  
Print name & status