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FEATURE

MORE SECRETS OF THE MMR SCARE

# Commentary: I see no convincing evidence of "enterocolitis," "colitis," or a "unique disease process"

Wording of Wakefield paper did not reflect the data shown in the grading sheets

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I reviewed the gastrointestinal histology grading sheets completed by Amar Dhillon[1] for 11 of 12 children with developmental disorders, who I understand were part of the clinical case series described by Wakefield and colleagues.[2] The article reported that all but one child had histology showing "non-specific colitis." It described patients as having enterocolitis and colitis, and said that the findings suggested a unique disease process.

With regard to the large bowel, a box labelled "non-specific" is ticked on one or more grading sheets for all children except one. In most cases this judgment is based on an increase in mononuclear cells in the lamina propria. However, lymphocytes and plasma cells are normally present in the lamina propria of the colon because the bowel mucosa is constantly challenged by dietary antigens and bacteria. This is physiological or controlled inflammation and is a sign that the bowel is working properly.[3] Minimal or mild inflammatory changes should not be reported as colitis,[4] and lymphoid hyperplasia is common in children. A change in distribution of inflammatory cells, with more cells in the basal part of the lamina propria, is a sign of abnormality, but this was not assessed on the sheets.[5] The abnormalities reported in the colon could be the result of many mechanisms, one being the preparation of the patients for colonoscopy.

For one child there is some evidence of inflammation, given that occasional polymorphs are present in the transverse colon, sigmoid colon, and rectum, together with some increase of mononuclear cells. However, the aetiology is unclear, and there are no positive diagnostic indications for considering inflammatory bowel disease. In two other children there are some polymorphs in the caecum or rectum. Overall, these changes could still have been caused by the preparation for colonoscopy. They could be classified as "focal active colitis," a condition which can be due to infections or other causes, and which in paediatric patients is related to inflammatory bowel disease in only a minority of cases. In the other children, the evidence is not sufficient for a diagnosis of colitis.

Data on the terminal ileum are reported in nine of the children. For seven of these, the pathologist has ticked a box labelled "normal." For an additional child, he has ticked "non-specific," apparently on the basis of a mildly reactive follicle. The sheet for another child does not have a tick for either category, but a reactive follicle is identified on the sheet. One duodenal biopsy is reported, with the sheet ticked "non-specific" and identifying a slight increase in mononuclear cells.

For the assessment of ileal lymphoid hyperplasia, it is essential to have several biopsies, which the grading sheets show were not taken. Peyer's patches with lymphoid follicles are constitutively present in the terminal ileum, and a study available at the time of the Wakefield paper reported that the mean number of patches containing more than five lymphoid follicles varied from 59 before 30 weeks' gestation to 239 at puberty.[6] So the presence of lymphoid follicles, even with a clear germinal centre, is not at all abnormal.

It is not clear what is meant by "non-specific" on the sheets. It could be non-specific changes or findings. If what is meant is non-specific colitis, this would be an error of judgment. This is also so where the sheets grade small bowel biopsies, where inflammation would be enteritis.

In general, the data are rather similar to the reports of the Royal Free hospital pathology service, which I reviewed for the *BMJ* last year.[7] Although minor abnormalities are noted in a minority of patients, I see no convincing evidence of "enterocolitis," "colitis," or a "unique disease process" being present in all patients. The Wakefield et al paper is obviously problematic and its wording does not reflect the data shown in the grading sheets.

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