or severity should receive close attention. The presence of associated symptoms, or of relevant issues in the family history, or the physical findings may each prove helpful in determining which children require further evaluation, and in deciding the most appropriate direction for investigation.

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- 1 Apley J. *The child with abdominal pains*. London: Blackwell Scientific Publications, 1975.
- 2 Apley J, Naish N. Recurrent abdominal pains: a field survey of 1000 school-children. *Arch Dis Child* 1958; 33: 165–70.
- 3 Bury RG. A study of 111 children with recurrent abdominal pain. *Australian Paediatric Journal* 1987; 23: 117–9.
- 4 Conway DJ. A study of abdominal pain in childhood. *Great Ormond Street Journal* 1951; 2: 99–109.
- 5 Stone RT, Barberp GJ. Recurrent abdominal pain in childhood. *Pediatrics* 1970; 45: 732–8.
- 6 Burbidge FJ, Huang S, Bayless TM. Clinical manifestations of Crohn's disease in children and adolescents. *Pediatrics* 1975; 55: 866–71.
- 7 Murphy MS, Eastham EJ, Jimenez M, Nelson R, Jackson RH. Duodenal ulceration – a review of 110 cases. *Arch Dis Child* 1987; 62: 554–8.
- 8 Lambert JP. Psychiatric observations on children with abdominal pain. *Am J Psychol* 1941; 98: 451–4.
- 9 McGrath PJ, Goodman JT, Firestone P, Shipman R, Peters S. Recurrent abdominal pain: a psychogenic disorder? *Arch Dis Child* 1983; 58: 888–90.
- 10 Walker LS, Greene JW. Negative life events and symptom resolution in pediatric abdominal pain patients. *J Pediatr Psychol* 1991; 16: 341–60.
- 11 Talley NJ, Piper DW. The association between non-ulcer dyspepsia and other gastrointestinal disorders. *Scand J Gastroenterol* 1985; 20: 896–900.
- 12 Van der Meer SB, Forget PP, Kuijten RH, Arends JW. Gastroesophageal reflux in children with recurrent abdominal pain. *Acta Paediatr* 1992; 81: 137–40.
- 13 Lasser RB, Bond JH, Levitt MD. The role of intestinal gas in functional pain. *N Engl J Med* 1975; 293: 524–6.
- 14 Lemann M, Dederding JP, Flourie B, Franchisseur C, Rambaud JC, Jian R. Abnormal perception of visceral pain in response to gastric distension in chronic idiopathic dyspepsia. The irritable stomach syndrome. *Dig Dis Sci* 1991; 36: 1249–54.
- 15 Cottrell CR, Snisky CA, Martin JL, Mathias JR. Are alterations in gastro-duodenal motility responsible for previously unexplained nausea, vomiting, and abdominal pain? *Dig Dis Sci* 1982; 27: 650.
- 16 Pineiro-Carrero VM, Andres JM, Davis RH, Mathias JR. Abnormal gastro-duodenal motility in children and adolescents with recurrent functional abdominal pain. *J Pediatr* 1988; 113: 820–5.
- 17 Drumm B. Helicobacter pylori. *Arch Dis Child* 1990; 65: 1278–82.
- 18 Drumm B, Sherman P, Cutz E, Karmali M. Association of Campylobacter pylori on the gastric mucosa with antral gastritis in children. *N Engl J Med* 1987; 316: 1557–61.

- 19 Van der Meer SB, Forget PP, Heidendal GAK. Small bowel permeability to ⁵¹Cr-EDTA in children with recurrent abdominal pain. *Acta Paediatr Scand* 1990; 79: 422–6.
- 20 Van der Meer SB, Forget PP, Arends JW. Abnormal small bowel permeability and duodenitis in recurrent abdominal pain. *Arch Dis Child* 1990; 65: 1311–4.
- 21 Black DD, Haggitt RC, Whittington PF. Gastroduodenal endoscopic-histologic correlation in pediatric patients. *J Pediatr Gastroenterol Nutr* 1988; 7: 353–8.
- 22 Glassman MS, Schwarz SM, Medow MS, et al. Campylobacter pylori-related gastrointestinal disease in children. Incidence and clinical findings. *Dig Dis Sci* 1989; 34: 1501–4.
- 23 Barr RG, Levine MD, Watkins JB. Recurrent abdominal pain of childhood due to lactose intolerance. A prospective study. *N Engl J Med* 1979; 300: 1449–52.
- 24 Wald A, Chandra R, Fisher SE, Gartner JC, Zitelli B. Lactose malabsorption in recurrent abdominal pain of childhood. *J Pediatr* 1982; 100: 65–8.
- 25 Hyams JS. Chronic abdominal pain caused by sorbitol malabsorption. *J Pediatr* 1982; 100: 772–3.
- 26 Hyams JS, Etienne NL, Leichtner AM, Theuer RC. Carbohydrate malabsorption following fruit juice ingestion in young children. *Pediatrics* 1988; 82: 64–8.

Commentary

Recurrent abdominal pain remains frustrating for both patient and doctor. This review draws attention to five organic disorders which can present with abdominal pain. At one time or another or from one author or another all of these have been suggested as possible causes for the periodic syndrome.

What is so interesting, and it can only be taken as a tribute to John Apley, is that despite greater understanding of these disorders the enigma remains. If physicians are to have guidance on how to manage individual patients with recurrent abdominal pain then it would be helpful if an unselected series of such patients were studied to discover what the incidence might be of the various conditions outlined by Murphy and whether treatment made any difference to the outcome. Only then would we know whether to go further than we currently do in investigating this mysterious complaint.

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Adoption, genetic disease, and DNA

Many paediatricians, both in hospital and in the community, have contact with children who are subject to the adoption process. For those who are medical advisers to adoption agencies their professional opinion is sought, usually in the assessment of a child before placement. The assessment includes family medical history, recognising the importance of genetic disease, although in many cases little or no information is available from the putative father. In most instances the gathering of information is heavily dependent on history taken by social workers, and on notes recorded by family doctors. If a genetic disease is highlighted during this process, before the placement, then appropriate investigations and counselling can be undertaken. If the disease emerges after the placement, however, there are no guidelines, either in law or practice, which address the issues of confidentiality that might arise.

A new dimension has been added to this area by the advances in molecular genetics that make it possible to

track faulty genes through families by linkage or mutation analysis. It is now accepted that these advances challenge traditional principles of medical ethics concerning an individual's right to confidentiality of information by virtue of the fact that we share our genes with relatives. Genetic information about an individual is potentially of direct interest to biological relatives, as highlighted by the Report of the Committee on the Ethics of Gene Therapy, section 4.15.¹ Delicate issues of confidentiality may arise where the possible retrieval of information is prevented by placement of a child from a biological family into an unrelated family by adoption, or when there is a need to trace long separated biological relatives who are at risk of genetic disease. These ethical issues are unique to adoption in so far as there is special consideration given to rights and confidentiality for the child, as well as the adoptive, and birth, parents, and the break from the biological family has been given legal sanction. Yet clinicians may increasingly face

medicolegal liability where failure to disclose is seen as negligence.² It is important that these issues are not overlooked in the current process of consultation about a review of adoption law in the UK. In fact, it should be an essential focus of consultation. The last guidelines in this specific area were published in 1982³ when the present technology was embryonic. Morris *et al* commented in 1988 on the specific issue of whether children for adoption, at 50% risk of Huntington's disease, should be tested before placement.⁴ The overall problem, however, is much broader than this, and it is international.

Legislation still favours 'sealed' adoption records in many of the states and provinces of North America, thus precluding adopted persons from obtaining any details about their birth family. By contrast, the law in Scotland,⁵ Finland, Israel, and Sweden has always made it possible for adopted persons at 17 or 18 years of age to gain access to information about their original birth records. In England and Wales, since 1975,⁶ it has become possible for adopted persons at 18 years of age, and after counselling, also to gain such information. From this they may trace their birth family. Such a change was a welcome trend towards openness for the weight of evidence indicates that adopted persons who inquire about their origins cope better when they know the truth, rather than experiencing fantasies and fears about the unknown.^{7,8} As public awareness of genetics is increasing there is no reason to believe this does not apply to 'genetic', as well as 'social', origins.

Assessing the size of the problem quantitatively is not easy because adoption statistics are not compiled uniformly between nations but those countries that have reliably registered large numbers of adoptions are: England and Wales (879 601 from 1927–90*), Scotland (84 428 from 1931–90*), West Germany (approximately 70 000 from 1977–84), and the United States (approximately 91 000 in 1957 and 174 000 in 1970).^{9,10} The figures for the United States include both in-country and intercountry adoptions, while the others are purely in-country, the numbers of which are now declining throughout the Western world. In contrast to the UK, Scandinavian countries and the Netherlands have practised an 'open-door' policy for intercountry adoptions and these numbers are increasing sharply. In the Netherlands, for instance, 14 586 intercountry adoptions were registered from 1970–85 but the annual total increased eightfold over this period.⁹ There are therefore today a very large number of adopted persons alive for whom the question of genetic disease may be important. Resolution of their dilemma, however, may not be possible, especially if they were placed across an international boundary. Population studies have provided consistent and reliable prevalence data for genetic disease. Baird *et al* showed that 5.3% of the population will have signs of a genetic disease by age 25 years.¹¹ Applying these figures to UK adoption statistics as an example, a minimum of 46 619 persons from a total of 879 601 adoptees in England and Wales (1927–90), and 4474 from 84 428 in Scotland (1931–1990), will develop a genetic disease, and the number will be much greater if all late onset multifactorial conditions are included, that is familial cancers and cardiovascular and autoimmune diseases.

A number of requests for advice from family members and professionals are being received about how to proceed as a result of a genetic disease coming to light within an adoption placement, which may have occurred years or even decades earlier. Such requests may involve the tracing of individuals whose location is unknown, who may be

ignorant of the adoption placement altogether, and who may see no benefit in having their privacy invaded with knowledge they did not seek. Clinicians who face these requests will need to proceed cautiously and sensitively in each case, as they have done hitherto, but these requests are likely to increase as the public becomes more aware of genetic services. Can anything be done to make more genetic information available to those who need it while also maintaining confidentiality and discretion? Is there a place for guidelines specifically for genetic disease as it affects the adoption process? We would argue that the following should be borne in mind.

Firstly, that *adopted persons*, who have always asked about family health records, will increasingly ask questions about their *genetic* as well as *social* origins. They will want answers to these questions for their peace of mind as individuals and as they face anxieties and uncertainties about childbearing themselves. Secondly, that *prospective adoptive parents* will increasingly seek assurances or information about possible defective genes in the child they are going to adopt. Thirdly, that the *biological relatives* of an adopted person will reasonably expect the same benefits from knowing their risk status, in the event that the adopted person develops a genetic disease, as would be available to them if the adoption had never taken place.

Five issues enter the debate and need to be addressed.

(1) The first and most crucial one is: who owns our genetic information? This question, being aired publicly in another context relating to the controversy over 'gene patents' and the Human Genome Project,¹² is the fundamental issue and the reason why debate is required. Is this information always private until the individual is willing to make it available to others, or should it be, *prima facie*, the right of certain concerned persons to have access to it? There is no simple answer even in routine practice.¹ The dilemma here is whether adoption, *a priori*, should be treated differently or not.

(2) Genetic history taking. For adequate genetic histories it is essential that leading questions are used. Documenting such detail is time consuming. In adoption medical examinations the family history is very important but currently often dependent on the social worker closely involved with the case. This is not a task for which these professionals have been trained. There is, therefore, a need for discussion aimed at achieving uniform standards in this important part of the process, recognising the need for access to genetic and other specialist services when indicated.

(3) Screening for genetic disease. There is currently great interest in screening for common genetic disorders. Cost-benefit analysis is a prime consideration for the population as a whole. Should different criteria, however, be considered for the screening of children to be adopted, and/or of their birth parents, so that the best monitoring, earliest intervention, and genetic counselling be available to them? (Such screening for fragile X syndrome is already being debated by adoption authorities in the UK.) If so, two main options might be considered: (i) screen only the birth parents to provide information for the adopted person later in life and (ii) screen all children for adoption for genetic diseases, taking account of racial and geographical origin. In this latter case the right of the individual to choose has been removed; there is already vigorous debate about the ethics of presymptomatic testing of children at risk of genetic disease.¹³ Under both of these options there are the further problems of confidentiality and the disclosure of positive findings to the wider biological family.

(4) Storage of DNA. DNA can be stored indefinitely at low temperatures and this is a way of making genetic

*Adoption was given legal status in England and Wales in 1926 and in Scotland in 1930.

information available for future use. With informed consent samples from the birth parents could be stored for the future benefit of the adopted person. This may obviate the need to trace the birth parents if genetic disease emerges later. Registering the storage of DNA would need to be centralised and access to it safeguarded by legislation but these are not insurmountable problems.

(5) Lastly, record keeping and tracing. Even if much of the above were considered desirable there will be instances where progress can only be made by finding one or more key individuals in the biological family. The quality of record keeping may be tested under these circumstances and raise the issue of devising better ways of tracing people's movements through life. However, proposals to improve such tracing are likely to provoke opposition as infringements of personal freedom.

We are left with no final solution to the questions of 'rights' and 'confidentiality of information' with respect to genetic medical history and DNA. Adoption is an example of a process where there is particular need for discussion and debate about the special moral and legal issues raised by molecular genetic techniques. It is an issue that will have repercussions world wide wherever the adoption of children by non-relatives is practised and legalised. In the meantime the legal framework in the UK is inadequate and there is no consensus about how to proceed when genetic disease emerges after an adoption placement. There is a clear need for an examination of this whole issue and a

broad based debate about how these conflicts of interest can be acknowledged and resolved.

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- 1 Report of the committee on the ethics of gene therapy. HMSO: London, January 1992: 15–6.
- 2 Pelias MZ. Duty to disclose in medical genetics: a legal perspective. *Am J Med Genet* 1991; 39: 347–54.
- 3 Carter CO, BAAF Working Party. In: Oxtoby M, ed. *Genetics in adoption and fostering*. London: British Agencies for Adoption and Fostering, 1982.
- 4 Morris M, Tyler A, Harper PS. Adoption and genetic prediction for Huntington's disease. *Lancet* 1988; 332: 1069.
- 5 Adoption of Children (Scotland) Act 1930.
- 6 Children Act 1975. Section 26: obtaining of birth certificate by adopted person.
- 7 McWhinnie AM. *Adopted children. How they grow up*. London: Routledge and Kegan Paul, 1967.
- 8 Schechter MD, Bertocci D. The meaning of the search. In: Brodzinsky DM, Schechter MD, eds. *The psychology of adoption*. Oxford: Oxford University Press, 1990.
- 9 Hoksbergen RAC, Gokhale SD. *Adoption in worldwide perspective*. Lisse: Swets and Zeitlinger BV, 1986.
- 10 Registrar General for Scotland. *Annual report of the registrar general for Scotland 1990*. Edinburgh: General Register Office, 1991: 142.
- 11 Baird PA, Anderson TW, Newcombe HB, Lowry RB. Genetic disorders in children and young adults: a population study. *Am J Hum Genet* 1988; 42: 677–93.
- 12 Bodmer W. Hands off the human gene! *Guardian* 3 April, 1992: 19.
- 13 Harper PS, Clarke A. Should we test children for 'adult' genetic disease? *Lancet* 1990; 335: 1205–7.

Iatrogenic deaths in hereditary fructose intolerance

The rarity of a disease provides little reassurance for those who suffer from it. Hereditary fructose intolerance (HFI) was described more than 35 years ago¹ but fatal cases (sometimes related to the medicinal use of fructose based intravenous solutions) continue to occur. Given that the disorder responds to dietary treatment and is compatible with a normal duration of life,² how do these tragedies arise?

Best known to paediatricians, HFI characteristically presents with vomiting, symptomatic hypoglycaemia, and failure to thrive during weaning or on transfer from breast milk to fruit juice or artificially sweetened feeds. The affected infant has feeding difficulties and episodes of disturbed consciousness or even hypoglycaemic seizures occur. Should administration of fructose, or the related sugars sucrose or sorbitol continue, chronic intoxication results: there is jaundice, liver enlargement, renal tubular dysfunction, and a haemorrhagic tendency accompanying hepatic failure that leads to death.^{2–4}

The abundance of sucrose and fructose in infant foods renders survival dependent on significant reductions of sugar intake: the mother may identify preparations that provoke symptoms or the infant itself develops an aversion to sweet tasting foods and drinks. Avoidance of sweet comestibles was noted by Chambers and Pratt who, first reporting 'idiosyncrasy to fructose' in a 24 year old woman, observed that she could take glucose without ill effect but did not enjoy the taste.¹ Before diagnosis, most adults with HFI ingest only a few grams of fructose or sucrose per day – a fraction of that consumed by healthy individuals – and dental caries is rare.⁵

None the less, they continue to suffer abdominal symptoms and hypoglycaemia intermittently as a result of accidental dietary indiscretions. Although chronic intoxication with fructose has been considered unlikely after institution of a restricted diet, rigorous studies in children with HFI show that growth retardation accompanied by biochemical abnormalities occurs unless dietary fructose is reduced to less than 40 mg per kilogram body weight per day.⁶

HFI is transmitted as an autosomal recessive trait with an estimated frequency of one in 20 000 live births.⁷ The disease is caused by genetic defects in the specialised enzyme of fructose metabolism, aldolase B.⁸ Aldolase B is expressed in the liver, small intestine, and proximal renal tubule where it facilitates assimilation of dietary fructose by catalysing the cleavage of fructose-1-phosphate.⁹ In the absence of fructose – either ingested as the free sugar or derived from sucrose or sorbitol – patients with HFI suffer no ill effects but exposure to small amounts of this sugar induces functional impairment, for example renal tubular acidosis,¹⁰ and eventually structural injury in the tissues that are sites for its metabolism.

The mechanisms of fructose toxicity are complex: intracellular sequestration of fructose-1-phosphate depletes the intracellular pool of free inorganic phosphate (as shown by ³¹P magnetic resonance spectroscopy in vivo¹¹) and these effects inhibit glycogenolysis and gluconeogenesis leading to refractory hypoglycaemia.^{2,12} Feedback inhibition of ketohexokinase reduces the further metabolism of fructose so that when the renal threshold is exceeded this reducing sugar