Editorial

Journal of Medical Genetics, 1984, **21**, 1–3

Lateral reading 4

TREATMENT FOR STARVATION MAY KILL (Newell J. *New Scientist*, 18 August 1983:471). LETTER (Millward J. *New Scientist*, 8 September 1983:714).

Genetic factors in kwashiorkor? Work at the Liverpool School of Tropical Medicine by Professor R Hendrickse and his colleagues makes it likely that kwashiorkor is caused by aflatoxins rather than by simple malnutrition, the toxin being derived from a fungus which grows on crops stored in hot, humid conditions—and it is in climates of this type that kwashiorkor flourishes. The theory is that some children are genetically incapable of detoxifying aflatoxins and the result is liver damage which makes the body incapable of coping with the high protein diet which is now the mainstay of treatment for kwashiorkor. The theory is testable in animals and, if substantiated, the treatment of the disease will be revolutionised; there would be campaigns to improve the storage of crops and possibly the development of a vaccine against the effects of aflatoxins. Another aspect of the research relates to malaria, for, curiously, children with kwashiorkor are more resistant to malaria. Consequently if kwashiorkor is eliminated malaria would increase, with all the headaches that this imposes.

On 8 September 1983 a letter appeared in the *New Scientist* criticising John Newell's article, particularly the title. Joe Millward, of the London School of Hygiene and Tropical Medicine, points out that while the prevention of aflatoxin poisoning is of vital importance it is not a substitute for rectifying the underlying cause of kwashiorkor. This is a provision of an adequate supply of basic foods and the economic wherewithal to purchase it.

THE EMERGING GENETICS OF HUMAN CANCER (Krontiris TG. *N Engl J Med* 1983;**309**:404–9)

This leader is tough going; it deals with oncogenes and the various ways in which they may be activated. Reproduction of the table and the relevant references (see below), the titles of which are very explanatory, seemed to me the best way of conveying the different messages. The new information will almost certainly lead to better classification of neoplasms and then to identifying the best treatment for a particular lesion. But why cannot someone look at the DNA of the palms of our Liverpool tylotic patients (see Howel-Evans W *et al. Q J Med* 1958;**27**:413–29), who we know will develop carcinoma of the oesophagus, and compare it with that from the palms of a non-tylotic sib? If no differences are found it would help to cool down the present excitement!

TABLE 2 *Potential mechanisms of oncogene activation.*

*Oncogene**	*Source (species)*	*Event*	*Consequence*	*Reference no*
ras^{H}	Carcinoma (human)	Base mutation in coding sequences	New gene product with altered activity	21 22
ras^{H}	Normal cells (human)	Altered promoter for RNA polymerase	Increased transcription of messenger RNA (normal gene product)	23
mos	Plasmacytoma (mouse) Burkitt's lymphoma (human)	DNA insertion, translocation (?)	Increased transcription of messenger RNA, new gene product (?)	24
myc	Burkitt's lymphoma Plasmacytoma (mouse)	Chromosome translocation	Altered messenger RNA, new gene product (?), new transcriptional/ translational controls (?)	25–28
abl	Chronic myelogenous leukaemia (human)	Chromosome translocation	Unknown, altered messenger RNA (?)	29
ras^{H}	Wilms's tumour (human) (?)	Chromosome deletion	Unknown, altered messenger RNA (?)	30

*The entries in the 'oncogene' column are the locus designations of human cellular genes that are homologous to retrovirus oncogenes. *ras*^{H} is the homologue of Harvey murine sarcoma virus, *myc* that of avian leukaemia virus MC-29, *abl* that of Abelson murine leukaemia virus, and *mos* that of Moloney murine sarcoma virus.

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'THROWBACKS' AND 'REVERSIONS'

Browsing through 'Reversion and Allied Phenomena' in *Heredity* (J Arthur Thomson. London: John Murray, 1908) I was struck by the good sense of his statement that "as a descriptive term . . . the word 'reversion' is useful . . . and entirely legitimate", but I agree that great care is necessary before one applies the term to ancestral characters which have been lying latent for generations and suddenly reappear.

Geneticists are often accused of being able to explain anything by 'modifiers' but it seems to me that in a naturally occurring butterfly species hybrid that I am investigating they might account for occasional non-Mendelian segregation. The modifiers suggested relate to the mimetic pattern in one of the parent species (*Papilio dardanus*). This is controlled by a supergene on a particular chromosome but, in addition, there is cast iron evidence that there are also unlinked modifiers on different chromosomes, and because they are unlinked to the supergene they may be present in the genome of all the mimetic females in a particular race—but in the absence of the supergene they are switched off. In the species hybrid the unlinked modifiers will come up against different modifiers from the other species, and we postulate that these may then become activated and produce exceptional insects in a non-Mendelian ratio. "Not original", you will say, but it seems to me that this particular hybrid is useful to test the theory. Any comments?

I know that 'throwbacks' in plants are ten a penny and can be explained by the vagaries of polyploidy, but is it not astonishing that two such different methods of speciation should have arisen in organisms that had a common origin?

A topic for a review? (The new fee is up to £75.)

MITOCHONDRIAL INHERITANCE (Egger J, Wilson J. *N Engl J Med* 1983;**309**:142–6)

It has always seemed to me remarkable that children so often show characters clearly inherited from their fathers, with maternal inheritance in its various forms being given increasing prominence. However, in this paper, the mitochondria come into their own in a disease which I had never heard of, known as mitochondrial cytopathy, characterised by short stature, muscle disorders, and ataxia, and sometimes chronic nephropathy. The authors have studied 30 pedigrees, in 27 of which exclusively maternal transmission occurred, but in three there was also paternal transmission in one generation. At least one member of six pedigrees was investigated by muscle biopsy and it was shown that they were deficient in respiratory enzyme complexes, which is characteristic of the disease. The occasional paternal transmission might be explained if certain enzyme subunits are coded for by nuclear DNA. The findings are relevant to a much more familiar disease, Leber's optic atrophy, in which again lack of a mitochondrial enzyme has been confirmed, though in this disease there have never been any well-documented examples of male transmission.

In the same issue (page 182) there is a good editorial on the structure, function, and replication of mitochondria.

NEURAL TUBE DEFECTS IN THE CAPE TOWN AREA, 1975–1980 (Cornell J, Nelson MM, Beighton P. *S Afr Med J* 1983;**64**:83–4)

Minerva, writing in the *British Medical Journal* (1983;**287**:431), was quick to pounce on this paper. She evidently had an early sight of it as it took me several weeks to get a photocopy. The gist of the findings is that during the period 1975 to 1980, 105 infants out of a total of 116 859 delivered at selected hospitals in the Cape Town area had a neural tube defect. The combined incidence of spina bifida and anencephaly in Whites was approximately 1 in 300 births, which is similar to that generally encountered in the UK. However, the incidence in other ethnic

groups was appreciably lower at 1 in 1250 and 1 in 2000 births for the Coloured (mixed ancestry) and Black groups respectively.

I had always thought of white South Africans as the best fed population in the world and it will be most interesting to hear what the periconceptional supplementationists have to say about the matter. They will certainly have spoken forcibly long before this appears in print.

DROSOPHILA TAKES OFF (Flavell A. Review article. *Nature* 1983;**305**:96–7)

Three papers in the August 1983 issue of *Cell* (which I have not so far been able to get hold of) describe experiments in which cloned genes were injected into the germ line of *Drosophila*. In general the inserted genes functioned normally, but they always occupied a different locus from usual. Though they were autosomal genes, when they were put into an X chromosome they still functioned and also behaved as X linked genes do in *Drosophila*, that is, in a male they made twice as much of the enzyme concerned, which is the way *Drosophila* solves its dosage compensation problem. The *Drosophila* findings are in sharp contrast to those in mice, where similar cloned genes have not functioned normally when put back into their hosts. From the point of view of genetic engineering one hopes that man behaves like *Drosophila*.

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