1957; Anderson et al., 1958; Richards, 1969; Smithells et al., 1976) that women who have ASB infants have a poor diet. The relevance of this observation to the present hypothesis needs careful consideration. One is tempted to suggest that poor maternal nutrition leads directly to poor embryonic nutrition and from there to ASB. The difficulty with this explanation is its apparent failure to deal with the relatively low concordance rates in twins. If maternal malnourishment (an excess of some toxin or a deficiency of some nutrient) directly caused ASB, why are both twins not usually affected? Logically, it seems that one is forced back to invoke the intervention of the placenta.

These considerations unfortunately give no clue to the identity of the agent causing ASB. However, they may suggest a slightly different direction for experimental teratology. Many agents seem to produce ASB in experimental litters, but experiments have been unsatisfactory in that usually only relatively small proportions of fetuses have been afflicted with the malformation. If the placenta is intervening between the agent and the malformation in the manner suggested here, the question to be first answered may be not “What will produce ASB?” but “What will cause early placental damage?”.

I am grateful to Dr Anne McLaren (MRC Mammalian Development Unit) for helpful discussion. I am supported by the National Fund for Research into Crippling Diseases.

William H. James
The Galton Laboratory,
University College,
London WC1

References


Reproduction in a woman with mosaicism

SIR,

Reproduction in a woman with mosaicism, in which the major cell line was 46,XX, and a few cells were 45,XX,t(21q21q), was recently published in the Journal of Medical Genetics (Mark et al., 1977). This woman gave birth to a son with Down’s syndrome, whose karyotype was 46,XY,–21,+t(21q21q). Karyotypes of lymphocytes from the woman and her husband were normal. Only after multiple tissues from the woman were analysed (skin, right ovary) were cells containing the 21q21q translocation detected. The percentage of cells containing the translocation was consistently less than 10%. A subsequent fetus was also found to have 46,XY,–21,+t(21q21q) and the pregnancy terminated.

Some years ago, we reported (Wilroy et al., 1969) a family in which two sibs with Down’s syndrome were thought to have de novo 21q21q translocations. After using banding techniques, the karyotype of one of the sibs was found to be 46,XX,–21,+t(21q21q). The second sib died before the advent of banding techniques. The karyotypes of lymphocytes of both parents were normal. A skin biopsy was obtained from the mother, but the father refused to be biopsied. Only after 436 cells were analysed from the skin biopsy of the mother did we find one cell with the karyotype 45,XX,t(21q21q).

We agree with Mark et al. that chromosome analyses of tissues, in addition to lymphocytes, should be performed on parents of more than one child with apparently de novo translocation (D-21 or G-21) Down’s syndrome, in an effort to detect mosaicism in the parent in which the abnormal cell line makes up only a small proportion of the total cell population. An even more prudent approach might be to monitor all future pregnancies of such parents by amniocentesis, even though the low percentage mosaicism is not detected. One might consider analysing the chromosomes of other tissues, in addition to the lymphocytes, of parents after the birth of only one child with an
Correspondence

apparently de novo translocation, and certainly amniocentesis could be offered to such parents to monitor any future pregnancy.

ROBERT S. WILROY, JR.,
ROBERT L. SUMMITT,
AND PAULA MARTENS
Departments of Pediatrics and Anatomy,
and the Child Development Center,
University of Tennessee Center for the Health
Sciences, Memphis, Tennessee, USA

References


This letter was shown to Dr Hon Fong Mark who writes: ‘I am grateful to Dr Wilroy et al. for their comments and am in complete agreement with their views.’

On the relation between malaria and G-6-PD deficiency: a reply

SIR,

We appreciate the opportunity to respond to the communication of Bottini et al. (p. 363 of this issue), especially as we feel that the apparent differences between these authors and ourselves are semantic to some extent. We hope here to clarify our views on the relation between G-6-PD deficiency and malaria.

Bottini et al. go to some pains to document the fact that G-6-PD-deficient haemolytic crises in hemizygous males were extremely serious events before modern medical treatment, and that the added stress of malaria could hardly have made the condition selectively advantageous. We agree. In our previous communication (Huheey and Martin, 1975) we drew an analogy between G-6-PD deficiency and sickle cell disease, with respect to resistance to malaria. Though all analogies may be pushed too far, we believe that ours is a useful one in understanding the selective forces at work on what, at first glance, may appear to be a strictly deleterious gene. To look for positive selection for the gene for G-6-PD deficiency in hemizygous males undergoing haemolytic crises is as hopeless as looking for positive selection for the haemoglobin S gene in homozygous subjects undergoing the crises of sickle cell anaemia. Rather, those people who will receive the most positive selection will be those in whom the manifestations of the disease are minimal and, perhaps, clinically undetectable. Clearly, we never intended that the haemolytic crisis per se was a positive, selective factor. Indeed, we pointed out in our previous communication (Huheey and Martin, 1975) that the interaction between favism, in the broad sense of the word (taken to mean a set of genes necessary for the disease), and G-6-PD deficiency could operate in the exerythrocytic stages of the life cycle, such as in the recurrent infection of the parenchyma cells of the liver by Plasmodium vivax.

The balanced polymorphism of haemoglobin A/haemoglobin S is maintained by strong, positive selection for heterozygotes having erythrocytes that do not sickle under normal conditions, but which apparently cannot support an infection of Plasmodium. Similarly, one should look for positive selection for the gene for G-6-PD deficiency among heterozygous subjects, which in the case of this sex-linked trait must be females. Indeed, Bottini et al. cite precisely this type of evidence. Luzzato et al. (1969) found that in the erythrocyte mosaicism that occurs in heterozygous females, the parasite rate was from 2 to 80 times higher in normal cells than in the deficient erythrocytes. This is precisely the kind of protective effect predicted by the G-6-PD hypothesis.

Finally, we cannot disagree with the statement of Bottini et al. to the effect that natural selection involves the interaction of the entire environment upon the total genome of the individual. In this regard, we think that the study of the mutual interaction of the genes responsible for sickle cell disease and other traits thought to be related to malaria, such as G-6-PD deficiency, β-thalassaemia, haemoglobins C, E, etc., will prove especially fruitful in the future.

J. E. HUHEEY AND D. L. MARTIN
Department of Chemistry,
University of Maryland,
College Park, Maryland 20742, USA

References


Reproduction in a woman with mosaicism.
R S Wilroy, Jr, R L Summitt and P Martens

doi: 10.1136/jmg.15.5.406

Updated information and services can be found at:
http://jmg.bmj.com/content/15/5/406.citation

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/