VAN DIE REDAKSIE : EDITORIAL

SPONTANE MISKRAAM

Die veelvuldigheid van vraagstukke wat in verband staan met die probleem van spontane miskraam, is betreklik onlangs weer deeglik bespreek deur 'n verteenwoordigende groep deskundiges.[1] Daar is toe aangetoon dat ten spyte van die feit dat die toestand so dikwels voorkom, daar baie fasette van die probleem is waaroor ons nog heeltemal onkundig is. 'n Poging is egter aangewend om die feite waarmee ons wel bekend is, in oorsig te neem.

Dit wil voorkom of daar ongeveer 'n 15%-kans is vir enige swangerskap om in 'n miskraam te eindig. Om te weet of dit die gevolg is van genetiese abnormaliteite wat patologiese ovums voortbring, en of dit te wyte is aan omgewingsfaktore wat òf patologiese ovums òf afwykende funksie van die uterus veroorsaak, is somtyds baie moeilik. Diegene wat meen dat genetiese abnormaliteite aan die wortel van die kwaad lê, wys daarop dat abnormale ovums in 52 - 73% van gevalle aangetref word. Alle gevalle van miskraam kan egter nie op hierdie grondslag verklaar word nie.

In die geval van 'n normale swangerskap is reis nie as sodanig 'n etiologiese faktor by miskraam nie. Ernstige trauma is egter wel 'n faktor, en toevallige snykundige behandeling gedurende swangerskap kan ook 'n rol speel. Om die rol van emosionele faktore onder gekontroleerde omstandighede vas te stel, is baie moeilik. Sommige deskundiges gee egter tog aan die hand dat psigiatriese hulp verleen moet word in gevalle waar miskraam herhaaldelik voorkom. Daar word gesê dat ongeveer een derde van alle miskrame (en twee derdes van alle voortydige bevallings) veroorsaak word deur funksionele afwykings van die miometrium, aangesien saamtrekbaarheid van die uterus afhang van en varieer volgens die konsentrasie van die hormone van die ovarium, en van estrogeen en progesteroon, of van epinefrien wat vrygestel word deur weefselbeskadiging of psigiese skok. Dit mag wel moontlik wees dat liggaamlike en emosionele trauma die endokrienomgewing verander asook die stowwe van die miometrium wat by saamtrekbaarheid gemoeid is, sodat sametrekkings van die uterus, bloeding van die buitenste vrugvleis, en miskraam by vatbare persone ontstaan.

Die voorkoms van abnormaliteite by miskraam-fetusse is baie hoër as by babas wat op tyd gebore is. Dit mag dus verleidelik wees om hieruit af te lei dat abnormaliteite verantwoordelik is vir die vroeë beëindiging van die swangerskap. In gevalle van ernstige abnormaliteite mag dit wel die geval wees, maar dit is moeilik om te bedink hoe 'n plaaslike abnormaliteit, soos byvoorbeeld 'n gesplete verhemelte, 'n miskraam kan veroorsaak. Dit is gevind dat die voorkoms van misvormde kinders (in 'n groep kinders wat gebore is na 'n dreigende miskraam voorkom is) nie groter is as in 'n groep waar daar geen miskraam was nie. Dit dui daarop dat abnormaliteite van die fetus waarskynlik nie in verband staan met daardie dreigende miskrame wat tot tyd voortgaan nie.

Baie aandag is al geskenk aan die probleem van die moontlikheid van meer miskrame nadat 'n miskraam voorgekom het. Skattinge van die moontlikheid varieer van 6 tot 20% met 'n gemiddelde van 10%. Dit is moeilik om die voorkoms van herkenbare miskraam in enige samelewing te bereken, aangesien onherkende vroeë miskrame nie bygereken kan word nie. Dit word gewoonlik (alhoewel dit nie noodwendig altyd korrek is nie) aanvaar dat 'n vrou wat een of meer miskrame gehad het, meer blootgestel is aan nog 'n miskraam as 'n vrou wat dieselfde aantal voltydse swangerskappe gehad het. Die syfers wat gewoonlik in hierdie verband aangehaal word, is die van Eastman wat op Malpas se metode hereken is, dat, as die totale voorkomssyfer van miskraam 10% is, dan is die kanse om 'n miskraam na een vorige miskraam te hê, 13% ; na twee, 37% ; en na drie 84%. Hierdie berekeninge is waarskynlik te hoog. Hulle stem nie ooreen met die empiriese bevindinge, wat nou beskikbaar en baie laer is nie, en wat verbasend konstant bly as die verskillende monsters van die samelewing wat gebruik is, in gedagte gehou word. Op grond van hierdie berekeninge wil dit voorkom dat die kanse op 'n miskraam na 'n vorige miskraam ongeveer 20% is, met slegs 'n geringe vermeerdering tot 25% soos die aantal miskrame toeneem. Hierdie syfer, 25%, is belangrik (in teenstelling met 84%) by die bepaling van die waarde van voorbehoedende behandeling in sulke gevalle.

Die neiging vir miskrame om meer by sommige vrouens voor te kom as by ander, skyn aan te dui dat sekere van die oorsake by herhaling kan voorkom. Dit is egter glad nie seker dat die neiging 'n biologies-anderse groep verteenwoordig wat konstitusioneel nie in staat is om swangerskappe te behou nie. Die neiging kan ook die gevolg wees van blywende faktore in die moeder se omgewing, van permanente gevolge van 'n tydelike omgewingsfaktor, of van moederlike of fetale gene waarvan sommige dominant en andere resessief kan wees. Daar bestaan baie min bewyse oor watter, indien enige, van hierdie meganismes, werklik etiologies beduidend is.

1. Danforth, D. N. (1959): *Clinical Obstetrics and Gynaecology*. New York: Paul B. Hoeber Inc.

CHROMOSOMES STILL ON THE MARCH — AUTOSOMAL TRISOMY

Deviations from the normal diploid chromosome number of 46 in man (aneuploids) have been recently described in a rather surprisingly large number of conditions associated with particular congenital defects. Abnormalities affecting the sex chromosomes include monosomy (as in gonadal-dysgenesis-with-female-body-form) and trisomy (as in Klinefelter's syndrome). Aneuploidy affecting the autosomes (non-sex chromosomes) has so far been in the nature of trisomy only.

Autosomal polysomy has seldom been observed in animals ; most instances have been recorded in *Drosophilia* spp.[1] In *D. melanogaster*, monosomy and trisomy for

chromosome no. 4 produces virtually no deviation from normality, though flies tetrasomic for this chromosome are inviable. In view of the apparent rarity of animal polysomy, the recent discovery of five different varieties of human autosomal trisomy seems surprising.* The probable reason for this discrepancy is that in man studies have been confined to phenotypically abnormal individuals selected from large populations. No comparable study has been performed in any other species.

The first recorded human autosomal trisomy was found in mongolism in 1959 by three separate groups of workers,[2-4] in which condition chromosome no. 21 was affected. Patau and co-workers[5] described trisomy for chromosome no. 15 in a mentally defective girl, who had trigger thumbs, polydactyly, capillary haemangiomata, harelip, cleft-palate, apparent anophthalmia, and a heart defect. Edwards and associates[6] described trisomy in chromosome no. 17 in association with odd face, webbed neck, heart defect and neonatal hepatitis in a female. Most remarkable was a clinically normal man who was the father of a mongol child. Fraccaro and co-workers[7] found that he was trisomic for chromosome no. 19.

Another case has been described by Hayward and Bower.[1] This was a boy of three years of age who was mentally retarded and suffered from frequent convulsions. A port-wine naevus covered the distribution of the first and second divisions of the right trigeminal nerve and there was buphthalmos of the right eye. X-ray of the skull revealed extensive calcification in the right parieto-occipital region. There were no features of mongolism — in fact the patient showed a completely characteristic Sturge-Weber syndrome. Bone marrow was cultured by the now standard method. In all the cells studied an extra small acrocentric chromosome was found which was identified as probably no. 22 (the smallest of all).

The mechanism of production of trisomy is chromosomal non-dysjunction, which may occur at mitosis or meiosis (reduction division). Mitotic non-dysjunction may occur during early cleavage in the developing embryo, or during pre-meiosis mitosis in the adult gonad. The first type should produce somatic autosomal mosaicism; the second aneuploid meiotic cells whose behaviour would parallel that of cells in which the non-dysjunction occurs during meiosis.

Non-dysjunction during meiosis may occur during the first or second division. Since the second division is essentially a haploid mitosis, the consequences of non-dysjunction at this phase are similar to those occuring during mitosis. Non-dysjunction at the first division may be produced by several different mechanisms. One of them is a failure of proper bivalent formation which may arise in three ways: (*a*) if the chromosome pair concerned are non-homologous, (*b*) from failure of pairing (asynapsis) between homologous chromosomes, and (*c*) from desynapsis (i.e. failure of chiasma formation after pairing). The first of these must depend entirely upon genetic properties.

Which of the various possible abnormal mechanisms accounts for non-dysjunction in any of the defects mentioned is quite unknown. Nor can we say for certain that a direct causal relation exists between chromosome aberration and clinical defect; the trisomy might merely be an accompanying phenotypic effect or, in some instances, a chance association. In mongolism, however, with a fairly uniformly abnormal chromosomal pattern, it is certainly tempting to believe that the autosomal trisomy is the cause of the abnormal phenotype.

* More have been described since this article was written.

1. Hayward, M. D. and Bower, B. D. (1960): Lancet, **2**, 844.
2. Böök, J. A., Fraccaro, M. and Lindsten, G. (1959): Acta Paediat., **48**, 453.
3. Jacobs, P. A., Baikie, A. G., Court-Brown, W. M. and Strong, J. A. (1959): Lancet, **1**, 710.
4. Lejeune, J., Gantier, M. and Turpin, R. (1959): C.R. Acad. Sci., **248**, 602.
5. Patau, K., Smith, D. W., Therman, E., Inhoorn, S. L. and Wagner, H. P. (1960): Lancet, **1**, 790.
6. Edwards, J. H., Harnden, D. G., Cameron, A. H., Crosse, V. M., Wolff, Frankhauser, G. and Humphrey, R. R. (1960): J. Exp. Zool., **115**, 207.
7. Fraccaro, M., Kaijser, K. and Lindsten, G. (1960): Lancet, **1**, 724.