



## News, Views and Comments

### Silent partners: twins with selective mutism

In 1986, Marjorie Wallace's riveting book, *The Silent Twins*,<sup>1</sup> alerted audiences to a fascinating and heartbreaking condition, now known as selective mutism (SM). The subjects of her work were identical twins, June and Jennifer Gibbons of London, whose delayed speech at age 3 years marked the beginning of withdrawal into a private fantasy world. Wallace's work drew comments and commentary from psychologists, educators, linguists, physicians and neurologists, including Dr Oliver Saks who called it 'an enthralling story, and a major source and study'. Publication of the book was followed by a BBC documentary that brought the twins' story home to hundreds of concerned parents trying to make sense of the seemingly inexplicable silence of their children. Some parents of twins were among them.

Over a decade later, behavioral and medical researchers have edged somewhat closer toward recognizing the defining features of SM, understanding the basis of its onset and identifying the means for its control. Nevertheless, much about the condition remains elusive. Selective mutism is rare, affecting only about 1 in 1000 school children – the chance that an affected child would be a twin is about 1 in 40 000 (1 person in 40 is a twin). Therefore, it is not a widely studied disorder, although a small cadre of investigators continue to provide crucial insights.

The essential feature of selective mutism is failure to speak in some situations despite adequate speech performance in other situations.<sup>2</sup> Another criterion is interference of the behavior with communication and with educational and occupational achievement. Diagnosis of SM also requires that failure to speak must persist for at least one month. The use of non-verbal features and/or brief monosyllabic utterances may be observed among children with this disorder. SM should not be confused with lack of familiarity with language used in social situations, or with embarrassment associated with com-

munication disorders or other developmental disabilities.

In September 1997, I met Dr E Steven Dummit III, a psychiatrist at St Luke's–Roosevelt Hospital Center in New York, who has investigated this rare condition.<sup>3</sup> He further explained that selective mutism is not considered a language disorder, but a social anxiety disorder, specifically an exquisite sensitivity to interactions with individuals outside the family. It is usually evident by about age 3 when children are in new verbally interactive settings, such as pre-school. Girls are affected twice as often as boys. Most of the 50 children evaluated in Dr Dummit's study came from middle class families. This condition was originally called elective mutism, but the name changed to selective mutism in 1994 to reflect the fact that individuals' failure to speak may be situation-dependent.

Over the years, I have heard from parents whose identical twins display SM. I was curious about this condition in view of twins' increased language difficulties.<sup>4</sup> Sue Newman and Carol Miller, both mothers of affected identical twin daughters, co-founded and co-direct the Selective Mutism Foundation, Inc.<sup>5,6</sup> This non-profit organization encourages research efforts by investigators and provides information and assistance to families in need. (Material can be obtained by sending a self-addressed envelope with two U.S. postage stamps or equivalent in international postal coupons to Sue Newman, PO Box 450632, Sunrise, FL 33345-0632, USA.)

Sue told me that approximately 20 families with affected twins have joined the organization – 350 people subscribe to the newsletter, but the organization has been contacted by hundreds more. Systematic twin research on selective mutism has not been undertaken, probably because the number of affected twins is small. Sue believes that both co-twins in all pairs thought to be identical are affected, whereas in many instances only one co-twin in pairs thought to be fraternal is affected. Should this observation be confirmed, it would suggest

genetic influence on the onset and persistence of SM.

A recent study by Ford, Sladeczek, Carlson and Kratochwill (1998) of 153 respondents out of 300 solicited members of the Selective Mutism Foundation yielded 15 twins (members of eight sets).<sup>7</sup> Five twins were from male–male pairs and ten were from female–female pairs. Parents of 14 of the 15 twins indicated the presence of SM (seven twins) or SM-like behaviors (seven twins). Twins' zygosity was not indicated, but would be of considerable importance for understanding genetic and environmental factors relevant to this disorder. At present, observations of selective mutism, anxiety disturbances, social phobias and shyness in the relatives of affected children are compatible with genetic influence.

A population-based study of 7–15-year-old children from two Swedish school districts identified five cases of SM (three girls and two boys), as well as 25 children whose shyness and reticence did not warrant a diagnosis of SM.<sup>8</sup> One of the two boys was a DZ twin whose twin brother was described as 'talkative' and 'very unlike "the silent one"'. His parents claimed he spoke at home, but not at school, and that he followed his brother around 'like a shadow'. Unfortunately, methods for determining zygosity were not provided. In this study, the SM rate was 18/10 000, higher than in most other studies. The investigators suggested that SM may occur more commonly than has been believed, given that children in this study had shown symptoms for at least a two-year period.

The possibility that twins suffer more frequently from selective mutism than non-twins is uncertain. Dr Dummit and his colleagues identified three affected identical twin pairs who comprised 12% of the individuals (or 6% of the families) in his study, exceeding the 2.5% of twin individuals and 0.8% of identical twin individuals in the population. Families with twins (5.7%) are also overrepresented among subscribers to the Selective Mutism Foundation's newsletter. Most behavioral disorders do not

occur more often in twins than in singletons. Twins affected with selective mutism may be more likely to attract professional attention than non-twins, elevating the numbers that get reported. Information on the twin–non-twin balance among families not receiving the newsletter would be helpful, as would population-based surveys of affected individuals.

It is possible that treating identical twins with selective mutism may be more difficult than treating fraternal or non-twins, due to their close social relations. A mother of affected 14-year-old identical girls, Kay Klatt, who contacted me in 1988, believed her daughters' mutual reinforcement of their language behavior explained its persistence. Dr Dummit agreed that this could happen, indicating that once the behavior begins 'it takes on a life of its own'.

Dr Dummit has reported encouraging results from treating affected children with the drug fluoxetine for a 9-week-period.<sup>9</sup> In his group of 215–14-year-old children, 76% showed improvement, namely reduced anxiety and increased speech in public places. Younger children showed better progress than older children. He has also treated several twin pairs, and finds that observing them when they are unaware reveals the flavor of what is going on between them. Some twins show 'secret signs', suggesting that they are closely attuned to what the other is thinking. Selective mutism is a rare disorder and should not be confused with the private words and gestures displayed by many young twin pairs.

## Medical Reports and Resources

### Stuck twin sign: a new view

The stuck twin sign is a curious label for a potentially life-threatening and controversial prenatal difficulty. It refers to the adherence of a diamniotic twin fetus to the intrauterine sidewall due to depletion (or near depletion) of amniotic fluid. The fetus is not literally 'stuck' on the intrauterine lining – instead, fetal movement is restricted by the embryonic membrane so, despite movement by the mother, the fetus appears to be 'stuck'. Dr Joseph RWax of the Hartford Hospital in Hartford, CT, explains that the stuck twin sign is a sonographic observa-

tion, rather than a diagnosis of what has taken place.

Controversy surrounding this condition comes from questions of etiological factors and diagnostic criteria. Resolving these issues has been difficult partly because most hospital centers encounter relatively few cases.<sup>10</sup> Some physicians believe that the stuck twin sign results from twin–twin transfusion, causing oligohydramnios (reduced amniotic fluid, leading to retarded fetal growth) in the 'donor' twin and polyhydramnios (increased amniotic fluid, leading to fluid accumulation in body tissues) in the 'recipient' twin. However, not all agree. Dr Wax and his colleagues recently argued that a stuck twin 'confirms neither monochorionicity nor monozygosity, as our case demonstrates. Dichorionicity or dizygosity should be considered if the co-twin is surrounded by a normal amniotic fluid'. His provocative paper, 'Fetal triploidy: a unique cause of the stuck twin sign', described chromosomally discordant twin fetuses (46, XX and 69, XXX) in which the stuck twin sign was detected in the triploid twin at the 17th gestational week.<sup>11</sup> The twins were most probably dizygotic, given their different chromosomal complements and the fact that the 46, XX co-twin had a normal amniotic fluid volume. The twins seemed to share the same placenta, but Dr Wax agrees it was most likely fused – early demise of the chromosomally aberrant twin (at 19 weeks) prevented examination of the placenta. He also advocates chromosomal analysis of the stuck twin when indicated, despite the perceived difficulties in so doing. He was able to obtain cells by amniocentesis, followed by infusion with saline solution which was then withdrawn for chromosomal study.

The appropriate criteria for stuck twin sign have also been debated. Post-natal indicators, such as a co-twin hemoglobin difference of 5 gm/dl, have been used but may not apply prenatally because the birth process may affect these findings.

When both fetuses are affected by the stuck twin sign, normal amniotic fluid volume may be restored by repeated amniocentesis.<sup>12</sup> Procedural difficulties can, however, interfere with the success of such interventions.

### Giant retinal tears: first case of MZ twin concordance

Perhaps the finest feature of twin research is that it suggests new ideas about old observations. In January 1999 researchers at the Bascom Palmer Eye Institute in Miami reported a case study of idiopathic giant retinal tears with retinal detachment diagnosed only two weeks apart in 40-year-old MZ female co-twins.<sup>13</sup> Genetic influence had been previously suggested by a report of sibling concordance for bilateral tears and an excess of retinal detachment (but without mention of bilateral tears) in 31 members of a 181-person, five-generation family from Texas. The presence of giant bilateral tears in both identical co-twins urges renewed efforts toward disclosing the sources of possible genetic effects.

A bothersome feature of this otherwise intriguing paper was the authors' neglect to describe the methods by which the zygosity of the twins was determined. I contacted a member of the research team (Dr Chaudry) who explained that this was based upon the twins' identical appearance – they were 'exactly alike, you could not tell them apart'. Of course an affirmative answer to the question, 'Is it hard for strangers to tell them apart?' diagnoses MZ twins with virtual certainty,<sup>14</sup> but this does not meet the standards of scientific rigor required for a single case report. (In contrast, misdiagnosis of an occasional pair in a large scale study would be unlikely seriously to bias the findings.) Most twin researchers have encountered exceptional DZ twins whose matched physical appearance proved misleading until blood was analyzed.

This particular episode recalled Race and Sanger's (1975) comment on James Shields' extraordinary ability to accurately classify twins based on global physical inspection: 'For many years, Mr James Shields of the Genetics Unit at the Maudsley Hospital has been sending us blood from the twins. We find that the blood groups practically never contradict the opinion of such a skilled observer of twins.'<sup>15</sup> I trust, however, that even seasoned twin watchers would hesitate to rely on their visual skills when classifying twins for scientific study, given the uncertainty this would introduce. Lack of certainty surrounding the zygosity of a twin pair in a case study can

make colleagues reluctant to accept the findings or to pool them with existing data.

At the risk of being intrusive, I forwarded copies of Nichols and Bilbro's Physical Resemblance Questionnaire to Dr Chaudry who accepted them with good grace.<sup>16</sup> I was, however, reassured to learn that there had been a previous caller with the same concern.

#### Twin transplants

It is well known that MZ twins share an ideal donor-recipient relationship when it comes to organ transplantation because of their matched immune systems. There are, nevertheless, examples of successful MZ twin organ transplants that are especially striking because they affirm the psychological, as well as biological, compatibility of the partners. At age 30, an anorchic male identical twin received a testicle from his co-twin in what appears to be the first transplant of its kind.<sup>17</sup> The normal co-twin had experienced normal puberty at age 13, in contrast to his twin brother who remained prepubescent at age 14, prompting a series of chorionic gonadotropin injections. Exploratory surgery then revealed an absence of testes, so at age 18 he began a regimen of depot-testosterone for induction of puberty. Five years were spent in search of a surgical team willing and able to perform a testicle transplant.

On 17 May 1999 the right testis of the normal twin was transplanted to the right scrotum of his twin brother.<sup>18</sup> His serum testosterone reached normal levels within two hours after surgery, and his sperm count reached 8–14 million with 30–50% motility within 8 months of surgery, indicating reproductive capability. Conception did not, however, occur for 2 years. An examination at the time of the transplant indicated that the twin's wife was fertile, yet re-evaluation 2 years later showed shortened luteal phases and extended follicular phases. This problem was medically corrected and the couple now have a healthy son.

The source of anorchia in this MZ twin pair remains speculative. A search through the medical literature suggests that this operation was the only one ever performed.

Early in 1999 identical twin doctors Rafael and Robert Mendez, and

patients Petra Martinez and Anna Cortez were involved in an unusual medical collaboration at the University of Southern California Hospital.<sup>19</sup> The female twins, aged 37, suffered from a genetic defect in which urine flowed back from their bladders to their kidneys. Surgical intervention in their teenage years proved successful for Petra, but less so for Anna who later developed chronic kidney infection. Petra was willing to donate a kidney to her sister and discovered the Mendez surgical team. It turned out that the brothers had performed joint transplant operations for 30 years, including surgery on two other sets of twins. Rafael usually removes an organ from the donor and Robert inserts it in the recipient.

The ease with which the twin sisters decided to have this operation underlines the special relationship most identical twins share. I believe a formal twin study of willingness and attitudes toward co-twin organ donation would be an informative test of behavior-genetic and evolutionary-based hypotheses concerning cooperation and affiliation. The physicians exemplify the similar genetically-based work skills and work values demonstrated in the twin literature. The behavioral and physical attributes of twins who work closely together have not yet been systematically assessed.

#### Octuplets

The December 1998 birth of the Chuku octuplets in Houston, Texas, has been heralded as a medical miracle and a reproductive misfortune. The oldest and smallest member of the set (a female named Odera), delivered 9 days before the others, died when 2½ weeks old. She weighed only 10.3 oz at birth. Her five sisters and two brothers survived, but showed severe growth retardation and consequent medical complications, including immature respiratory functions and poor control of body fluids and chemicals. All infants have required intense hospital care before going home. They are at high risk for developing learning disabilities and a range of physical handicaps.

Much has been written in the professional and popular press about the promise of new reproductive technologies to assist infertile couples to

produce children. The pitfalls of these new procedures seem, however, to have been less widely aired in the general media than in the medical press. A recent essay, 'Eight is too many: the case against octuplets', in the 25 January 1999 issue of *The New Republic*,<sup>20</sup> by Ezekiel J Emanuel MD, PhD, Chairman of the Department of Clinical Bioethics at the National Institutes of Health in Bethesda, forces a hard look at the physical, emotional and societal costs of procedures leading to higher order multiple births. For example, the costs of premature infants' medical care often continue as they face constant difficulties during development. Parental time-sharing among seven same-age infants and toddlers is emotionally draining to all parties involved. According to Emanuel, 'The birth of octuplets ... is not a chance event; it is the result of deliberate actions by physicians, parents and society'. He applauds the efforts of medical specialists who use new medical technologies that bring children to childless couples. At the same time, he calls for a media curb on glorifying septuplet and octuplet births, reminding us that 'in this case, bigger may not be better – indeed, it may actually be worse'.

#### Gemini Holdings

Cambridge, England may hold the world's largest repository of medical and clinical data on MZ and DZ twins. Chief Executive Dr Paul Kelly, who founded this company 4 years ago, explains that there are 500–1500 pieces of information on each individual of which some material dates from 17 years previously. The number of twins entered in this massive registry now exceeds 10 000. Collaborators include 19 academic and clinical centers around the world. Access to Gemini Holdings is facilitated through various arrangements. This information was drawn from Dobson R.<sup>21</sup>

#### Twins around the world: arts, attitudes and athletics

Teheran, Iran

A new film, *The Apple*, documents the tragic life events of 12-year-old identical female twins, Massoumeh and

Zahra Naderi, confined to their home since the age of 12 by their 65-year-old father and blind mother.<sup>22</sup> When discovered by social workers in the summer of 1997, the twins appeared unwashed, unintelligible, mute and physically impaired. I have yet to see this film but wonder if the twins developed their own private words or gestures known to characterize many twins (mostly identical) who are reared in close proximity during the early years. I also wonder to what extent having a twin helped buffer each sister from their devastating surroundings.

Film-maker Samira Makhmalbaf (who was only 18 years old at the time) captured the twins' situation as naturally as possible by recreating home situations and allowing the family to act naturally. The twins have since been transferred to a child welfare agency where, according to Makhmalbaf, 'the more they come into contact with society, the more complete they became as human beings'. She sees the twins' change in life circumstances as emblematic of the situation facing Iranian women – they live in a society that restricts the freedom and energy they have the potential to express.

The Apple was positively reviewed at the 1998 Cannes Film Festival and was part of the Fall 1998 New York Film Festival before opening in New York in February 1999.

#### Saravena, Columbia

The U'wa tribe, which numbers approximately 5000, sees twins as 'a damnation and a product of "impure spirits"'. Such beliefs underlie the ritual killing of one or both twins in some cultures, a practice that has occurred among this South American tribe located in Saravena, Columbia. In February 1999 news that a mother had abandoned her newborn male-female twin pair drew concerned attention from international news services.<sup>23</sup> Local sources (considered credible) claimed that the twins' death was imminent, although village elders denied this, explaining that ritual killing of twins was practised only in the past. They indicated that the twins were being cared for by the Institute of Family Welfare in Saravena.

The birth of twins has inspired joy, fear and uncertainty in cultures around the world. These different atti-

tudes and their consequences have been examined in two recent reviews by University of Durham investigators.<sup>24,25</sup> They concluded that factors prompting twin infanticide do not differ from those prompting non-twin infanticide, eg survival or population control. Human ethologist Eibl-Eibesfeldt reminds us that there is 'no society known in which mothers kill their own child lightheartedly, for an inhibition against killing must always be overcome'.<sup>26</sup>

#### Descoberto and Sao Joao, Brazil

These small Brazilian towns north of Rio de Janeiro are home to the family of twins, Ronaldo and Romildo da Costa. In September 1998, 28-year-old Ronaldo made headlines around the world by completing the Berlin marathon (26.2 miles) in 2 hours 6 minutes and 5 seconds, setting the world record for the fastest race at that distance.<sup>27</sup> He trained formerly with his twin brother, but now pays his nephews to pace him riding their bicycles. I was eager to know if these twins were identical or fraternal. According to da Costa and his agent, Luis Posso, the twins are fraternal – they are 'very different, never confused'. The twins differ in height by three-quarters of an inch and differ in weight by 13 lbs, information that did not help settle the zygosity question. Among the criteria in Nichols and Bilbro's 1966 questionnaire for classifying twins as MZ or DZ, are the following: twins must differ in height by 1½ in and in weight by 15 lbs for classification as DZ at the second highest certainty level.<sup>28</sup> I would therefore hesitate to include da Costa in formal twin research until his zygosity could be confirmed.

Twins are making substantial contributions to our understanding of genetic and environmental factors underlying sports performance. I plan to survey this work in forthcoming issues.

#### References

- 1 Wallace M. *The Silent Twins*. Prentice Hall: NY, 1986.
- 2 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. APA Press: Washington, DC, 1994.

- 3 Dummit ES III et al. Systematic assessment of 50 children with selective mutism. *J Acad Child Adolesc Psychiatr* 1997; 3: 653–660.
- 4 Segal NL. *Entwined Lives: Twins and what they tell us about human behavior*. Dutton: New York, 1999.
- 5 Miller CM, Newman S. *Understanding Selective Mutism*. Selective Mutism Foundation Inc, 1997.
- 6 West HI. The Silence of the Lambs. *New York Daily News* 9 September 1991, p 23.
- 7 Ford MA, Sladeczek IE, Carlson J, Kratochwill TR. Selective mutism: Phenomenological characteristics. *School Psychol Qly* 1998; 13: 192–227.
- 8 Kopp S, Gillberg C. Selective mutism: A population-based study. *J Child Psychol Psychiatr* 1997; 38: 257–262.
- 9 Dummit ES III et al. Fluoxetine treatment of children with selective mutism: An open trial. *J Acad Child Adolesc Psychiatr* 1996; 35: 615–621.
- 10 Berry SM et al. Comparison of intra-uterine hematologic and biochemical values between twin pairs with and without stuck twin syndrome. *Am J Obstet Gynecol* 1995; 172: 1403–1410.
- 11 Wax JR, Steinfeld JD, Ingardia CJ. Fetal triploidy: A unique case of the stuck twin sign. *Obstet Gynecol* 1998; 92: 2.
- 12 Sabbagha RE. Pregnancy dating and evaluation by ultrasonography. In: Keith LG, Papiernik E, Keith DM, Luke B (eds). *Multiple Pregnancy: Epidemiology, Gestation and Perinatal Outcome*. Parthenon: New York, 1995.
- 13 Chaudry NA, Flynn HW Jr, Tabandeh H. Idiopathic giant retinal tears in identical twins. *Am J Ophthalmol* 1999; 127: 96–99.
- 14 Cohen DJ, Dibble E, Grawe JM, Pollin W. Separating identical from fraternal twins. *Arch Gen Psychiatr* 1973; 29: 465–469.
- 15 Race RR, Sanger R. *Blood Groups in Man*, 6th edn. Blackwell: Oxford, 1975.
- 16 Nichols RC, Bilbro WC Jr. The diagnosis of twin zygosity. *Acta Genet Statist Med* 1966; 16: 265–275.
- 17 Silber SJ. Transplantation of a human testis for anorchia. *Fertil Steril* 1978; 30: 181–187.
- 18 Silber SJ, Rodriguez-Rigau LJ. Pregnancy after testicular transplant: Importance of treating the couple. *Fertil Steril* 1980; 33: 454–457.
- 19 Pool B. Twin doctors and their patients celebrate. *Los Angeles Times* 26 January 1999; A-13R.
- 20 Emanuel EJ. Eight is too many: the case against octuplets. *The New Republic* 25 January 1999; 8: 10–11.
- 21 Dobson R. British twin database to be floated. *Br Med J* 1999; 318: 79.
- 22 Camhi L. Daughter of Iran, shades of her father. *New York Times* 21 February 1999.

- 23 Reuters News Service. Indians in Columbia deny they plan to sacrifice newborn twins. 20 February 1999.
- 24 Box HL, Hill CM. Reevaluating 'twin infanticide'. *Curr Anthropol* 1996; 37: 856–863.
- 25 Hill CM, Ball HL. Abnormal births and other 'ill omens'. *Hum Nat* 1996; 7: 381–401.
- 26 Eibl-Eibesfeldt I. *Human Ethology* Aldine de Gruyter: New York, 1989, p 711.
- 27 Longman J. Brazilian shatters world record marathon by running 2:06:05. *New York Times*, 24 September 1999.
- 28 Nichols RC, Bilbro WC Jr. The diagnosis of twin zygosity. *Acta Genet Statist Med*, 1996; 16: 265–275.

Nancy L Segal  
Department of Psychology  
California State University  
Fullerton, CA, USA  
nsegal@fullerton.edu

### School placement of multiples

The number of multiple births in the United States and worldwide continues to grow. These multiples require special social and psychological considerations with regard to their education. With this in mind, the National Organization of Mothers of Twins Clubs, Inc. (NOMOTC), a multiple birth organisation in the United States of America, has developed a set of Guidelines for the Education of Multiple Birth Children. Aimed at educators and school support staff, the policy statement outlines the special academic, social and emotional needs that multiple birth children can have in an educational setting.

Specifically, these guidelines address seven areas that both educators and parents should consider in order to ensure the best possible educational settings for multiple birth children. Most importantly, NOMOTC suggests 'schools should provide an atmosphere which respects the close nature of the multiple bond while at the same time encouraging individual abilities'.

Unfortunately, looking at multiples individually is not always the case. A research study, conducted by NOMOTC, revealed that educators believe 35% of all multiples should be separated in school, with the highest percentage choosing kindergarten as the point of separation; 66% of multi-

ples in the survey completed by their mothers were separated at some time in their schooling.

Parents opinions can vary. Some parents believe that keeping their multiples together can help them achieve the greatest academic and social gains; others see separate classroom placements as a way to avoid or diminish competition between multiples. Often, the separation issue hinges on the unique interaction and personalities of the multiple set. Because of this, the NOMOTC policy advises 'schools should maintain a flexible placement policy throughout the early elementary years'.

'Placement decisions should not be made for the purpose of promoting the children's individuality or for the teachers' convenience and ease of name/face recognition. Successful placement involves a collaborative decision', the policy says. In other words, the policy suggests that educational institutions refrain from having an inflexible position with regard to school placement. Instead, NOMOTC recommends that the needs of the children in each set of multiples be considered individually. To achieve this end, the decision requires parental input. 'Parents can offer insights which will enable the educator to respond in a more effective manner to the needs of the children', the policy says.

The multiple bond among twins, triplets, or more can be affected by other academic decisions, such as retention or recommendation for special services, such as Gifted or Learning Disabilities Programmes. According to the policy, 'teachers need to be sensitive to the feelings and actions of all co-multiples and alert to possible problems for all the children'. In addition, the guidelines state, 'the effects of school retention... are much greater on a multiple birth child since they may alter the sibling relationship in a profound manner', and 'educators should move with extreme caution when considering... (such decisions).'

With the current rise in the rate of multiple births, educational issues surrounding multiple birth children are certain to become more prevalent. For these reasons, NOMOTC finishes its guidelines with a call for schools and districts to offer more opportunities for staff to learn about the special

considerations surrounding the education of multiple birth children. It further suggests that education-related courses at the university level include 'research findings into the psychology of twins and higher order multiples'.

In addition to these newly-prepared guidelines, NOMOTC publishes a booklet on the issue of school placement. A new research project has been launched to gather more information on educational issues with regard to multiple birth children. Further information can be obtained by directly contacting NOMOTC.

Rebecca Moskwinski MD  
c/o NOMOTC  
PO Box 23188  
Albuquerque, NM 87192, USA  
NOMOTC@aol.com

### Reduction of Grand Multiffoetal Pregnancies to Twins

The reduction of triplets or higher multiples to twins (multiffoetal pregnancy reduction: MPR) described for the first time by Dumez and Oury in 1986<sup>1</sup> probably does not increase perinatal risk and/or pregnancy complications. This conjecture was recently confirmed in two independent investigations by a group of Greek and a group of US clinical investigators. Antsaklis et al<sup>2</sup> compared 158 twin pregnancies, left after foetal reduction with 135 normal twin pregnancies. These two groups appeared not to differ significantly in the number of miscarriages, mean gestational age, birth weight of the twins, and perinatal mortality rate. Similar results were reported by Selam et al<sup>3</sup> who studied a cohort of dichorionic twin pregnancies who reached 24 weeks of gestation and were delivered in a New York hospital between 1986 and 1997. This cohort appeared to contain 77 multiffoetal pregnancies that were reduced to twins, and 140 non-MPR twin pregnancies. These two groups were compared in respect of several pregnancy complications and neonatal outcome characteristics. MPR twin pregnancies were similar to non-MPR pregnancies, except for Caesarean section rates (higher in MPR pregnancies) and neonatal polycythaemia (an increase in red cell mass caused by sustained

overactivity of the erythroid component of bone marrow, which may occur as a compensatory physiological response to tissue hypoxia).

### Genetics of Blood Pressure: Renin and Angiotensin-Converting Enzyme

Renin is an enzyme that is synthesised as inactive prorenin in the kidney and released into the blood in the active form by, amongst others, renal sympathetic nerve activity, circulating catecholamines, blood pressure decrease and sodium depletion. It catabolises the formation of angiotensin-I from angiotensinogen or renin substrate (a serum  $\alpha_2$ -globulin secreted in the liver). Angiotensin-I in turn is transformed to angiotensin-II by the angiotensin-converting enzyme (ACE). Angiotensin-II is a very potent vasoconstrictor agent and is thus important in the complex blood pressure regulation mechanism.

Italian and Polish scientists (Rossi et al<sup>4</sup>) have tried to shed some light on the genetic influences on plasma levels of ACE (pACE), plasma renin activity (PRA), and ambulatory blood pressure (ABP) by combining genetic epidemiological and molecular genetic information. They did this by studying MZ and DZ twins and measuring not only the phenotypes mentioned but also by genotyping the DNA-polymorphism for ACE with two alleles: D(letion) and I(nsertion). Substantial heritability (stronger association in MZ than in DZ pairs) was found for pACE but not for PRA. DD subjects had significantly higher pACE levels than II subjects, DI's being intermediate. Renin was not associated with the pACE genotype. The combination of these results suggests that renin may be under relatively strong control of environmental conditions.

### Obesity: the Effect of Sport

The prevalence of obesity (defined by WHO as a Body Mass Index, BMI, larger than 30) has been gradually increasing in Western societies in the past 10 years. This suggests considerable influence of environmental factors that somehow affect this health-

threatening condition, more prevalent among women than among men.

Twins can help to improve our insight into the extent to which overweight and obesity is a genetically-based condition that one cannot escape from, and to what degree behavioural and environmental influences are responsible. Australian and British epidemiologists (Samaras et al<sup>5</sup>) have investigated 241 healthy female MZ twin pairs and 228 healthy female DZ pairs. From these 938 subjects, 65% had normal weight (BMI between 20 and 24.9), 30% were overweight (BMI between 25 and 29.9) and 7% were obese (BMI greater than 30). Seven per cent were underweight (BMI less than 20). The investigators measured total body fat, central abdominal fat – thought to be the most risky for the development of cardiac heart disease, physical activity, dietary intake, social class, whether the woman was taking hormone replacement therapy (HRT), and smoking habits. The authors did not apply the usual MZ and DZ intraclass correlation comparisons but calculated the effects of all independent factors on within-pair differences in body fat in MZ twins, thus keeping genetic contributions constant.  $G \times E$  interaction was analysed by defining each twin's fat genotype as the fat phenotype of the co-twin. (One should not exclude the possibility that this latter method of applying genotype, especially by not taking zygosity into account, can lead to unreliable and inconclusive results.

It was found that of all measured parameters, physical activity was the strongest predictor of both total fat and central abdominal fat. MZ pairs who were discordant for sports activity showed the largest difference in body fat, allowing for the influence of other measured factors. Mobility is thus more important than eating! Subjects with a genetic disposition to obesity benefited equally from physical activity as those without such a disposition.

### References

- 1 Dumez Y, Oury JF. Method for first trimester selective abortion in multiple pregnancy. *Contr Gynecol Obstet* 1986; 15: 50.

- 2 Antsaklis AJ, Drakakis P, Vlazakis GP, Michalakis S. Reduction of multifetal pregnancies to twins does not increase obstetric or perinatal risks. *Hum Reprod* 1999; 14: 1338–1340.
- 3 Selam B, Lembed A, Stone J, Lapinski R, Berkowitz RL. Pregnancy complications and neonatal outcomes in multifetal pregnancies reduced to twins compared with nonreduced twin pregnancies. *Am J Perinatol* 1999; 16: 65–71.
- 4 Rossi GP, Narkiewicz K, Cesari M, Winnicki M, Bigda J, Chrostowska M, Szczech R, Pawlowski R, Pessina AC. Genetic determinants of plasma ACE and renin activity in young normotensive twins. *J Hypertens* 1999; 17: 647–655.
- 5 Samaras K, Kelly PJ, Chiano MN, Spector TD, Campbell LV. Genetic and environmental influences on total-body and central abdominal fat: The effect of physical activity in female twins. *Ann Intern Med* 1999; 130: 873–882.

### Heritability of Parkinson's disease

During the last couple of decades, many investigators of Parkinson's disease (PD) have focused on a possible environmental etiology, such as a particular form of intoxication or an infection by some virus. The search for a genetic basis was discouraged because of the low degree of concordance in MZ twins, equalling that in DZ twin pairs. This latter outcome was re-affirmed in a recent study by a group of US PD-researchers<sup>1</sup> who investigated PD in a group of nearly 20,000 male twins registered in the (US)WWII Veteran Twins Registry. In this group 193 twins appeared to have PD. Concordance rates (= co-twin is affected too) were similar for both MZ and DZ twins, viz. 0.155 in MZ and 0.111 in DZ pairs. In addition – and this is the scientific news – the authors found that in 16 twin pairs with PD that was diagnosed before the age of 50 years in at least one of the pair, concordance was 1.0 in four MZ pairs and 0.167 in the remaining DZ pairs. Though these numbers are small, the authors conclude that the contribution of genetic factors is absent if the disease begins after age 50 years but that genetic factors may be important in case of early onset (before age 50) PD.

Autosomal recessive juvenile parkinsonism has recently been mapped

to 6q25.2-q27 by investigators from Columbia University<sup>2</sup>.

### Breast cancer risk in twins

Finnish epidemiologists<sup>3</sup> have confirmed the earlier (surprising) finding that breast cancer risk in MZ female twins is significantly lower than that in DZ female twins (relative risk = 0.78). The risk in DZ twins did not differ from that in the general population. The researchers who did their longitudinal analysis in 13,176 female twins between 1976 and 1995, have no clear cut explanation for this difference and speculate on the possible influence of prenatal and/or postnatal behavioral protective conditions in MZ females.

### Twin data at odds with Barker hypothesis?

Prenatal, especially nutritional, conditions, are supposedly associated with adult pathological effects. This relationship is known as the fetal origin hypothesis, formulated by and mentioned after the British (Southampton) epidemiologist David Barker. Several of the key publications of Barker and co-workers, illustrating and supporting that hypothesis, were republished

in a book by the British Medical Journal (BMJ) in 1992: *Fetal and Infant Origins of Adult Disease*<sup>4</sup>. One of the convincingly documented associations in support for the Barker hypothesis concerns the negative relationship between birth weight and (adult) blood pressure.

The existence of such a relationship seems not to hold for twins however, as suggested by a recent research report from a New Zealand team of epidemiologists<sup>5</sup>. They measured, amongst others, blood pressure in a group of 795 nine-year old children from whom birth weight was known. From these children 22 were twins. The Barker hypothesis was confirmed for the 773 singletons but not for the twins: though the twins weighed on average 0.88 kg less than the singletons – which is compatible with many other observations – their blood pressure appeared to be 5.09 mm Hg less than that of singletons. The investigators do not mention whether this unexpected outcome holds too when the birth weight-blood pressure association is calculated within the twin group only, which is a necessary step for a definite test. When such a test would confirm the fetal origins hypothesis, then one could consider that as an indication that low birth weight in twins has a different etiology than that in singletons. Testing within the twin group is very likely impossible because the group is too

small, especially so since the 22 observations can not be considered as independent.

### References

- 1 Tanner CM, Ottman R, Goldman SM, Ellenberg J, Chan P, Mayeux R, Langston JW (1999). Parkinson Disease in twins. An etiologic study. *J Am Med Assoc*, 281, 341–346.
- 2 Jones AC, Yamamura Y, Almasy L, Bohlega S, Elibol E, Hubble J, Kuzuhara S, Uchida M, Yanagi T, Weeks DE, Nygaard TG (1998). Autosomal recessive juvenile parkinsonism maps to 6q25.2-q27 in four ethnic groups: detailed genetic mapping of the linked region. *Am J Hum Genet*, 63, 80–87.
- 3 Verkasalo PK, Kaprio J, Pukkula E, Koskenvuo M (1999). Breast cancer risk in monozygotic and dizygotic female twins: A 20-year population-based cohort study in Finland from 1976 to 1995. *Cancer Epidemiol Biomarkers Prev*, 8, 271–274.
- 4 Barker DJP (Ed.) (1992). *Fetal and Infant Origins of Adult Disease*. London: BMJ.
- 5 Williams S, Poulton R. (1999). Twins and maternal smoking: ordeals for the fetal origins hypothesis? A cohort study. *Br Med J*, 318, 897–908.

Jacob F Orlebeke  
Department of Biological Psychology  
Vrije Universiteit  
Amsterdam, Netherlands