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# LETTER

## Terminology for twin zygosity

Even in the pages of this august professional journal for twin researchers, I have noted a creeping tendency to use inexact terminology concerning two zygosity. I disagree with the use of the terms 'identical' and 'fraternal' instead of MZ and DZ. My objections stem from linguistic, logical and practical points of view.

'Frater' is the Latin for 'brother', and its use for female/female or female/male DZ twins is objectionable because it is prejudicial and demeaning to females. The only 'fraternal' twins are male/male twins (whether MZ or DZ) and the male twin of a male/female pair.

Parents are completely confused about the use of the word 'identical' instead of 'MZ' because they interpret the word literally to mean 'absolutely identical in every detail'. This is the sense in which we all use the word in other contexts, and it is therefore true to state that there are no such entities as 'identical' twins. For many years, I have been answering e-mails, talking at twin clubs and offering zygosity testing when zygosity is in doubt. It is very infrequent for parents of DZ twins to ask for testing. Just occasionally, a DZ twin pair has such strong familial resemblance that zygosity testing is indicated. More than 99% of requests for zygosity testing yield MZ results. The reasons are plain.

There are prenatal genetic, epigenetic and environmental effects on development that ensure that MZ twins are never 'identical'.[1] In fact, MZ twins show a far greater phenotypic range of concordance/discordance than do DZ twins.

Genetic discordances include the most phenotypically discordant MZ twins who are the pump and acardiac twins of reversed arterial perfusion; these twins are always MC and therefore always MZ. About 50% of acardiac twins have abnormal chromosomes, whereas the corresponding pump twins are usually normal. Heterokaryotypia is well known in MZ twins. Striking examples include cases where a 46,XY zygote maintains a 46,XY cell line, but there is also a 45,X cell line (as a result of post-zygotic mitotic non-disjunction/anaphase lag). The resulting Turner-Ullrich twin has female gonads and internal and external genitalia, but is MZ to the male twin. MZ twins can also be discordant for 21, 18 and 13 trisomies. MZ twins who are concordant for trisomy may be quite discordant for the phenotypic severity of that trisomy. Female MZ twins can show such different degrees of X chromosome inactivation that one has an X-linked genetic disease (such as Duchenne muscular dystrophy), whereas the other is quite normal. MZ twin males with X-linked mental retardation may show different expansions of trinucleotide repeats, resulting in different phenotypic severity. MZ twins with autosomal dominant genetic disorders may show phenotypic discordance for severity of expression. Among the epigenetic effects are the observation that MZ twins are usually (though not always) discordant for major malformations.

Environmental prenatal and perinatal events include all the effects of monochorionicity on fetal growth and development. No-one would deny that the donor or recipient of twin transfusion are MZ, but no-one could say that they resemble each other closely. And twin transfusion occurs in at least 10% of MC twins! It is notable that first-born twins of HIV-positive mothers are more likely to acquire HIV in the birth canal transit than are second-born.

Whereas these examples of discordance may be thought to be unusual, extreme and freakish, not representing the 'norm', I believe that they are the tip of an iceberg of many prenatal events that affect MZ twin development, making them considerably less than 'identical'. In varying degrees, often in rather subtle ways, they differentially affect development of all MZ twins. Yet many people will mislead twins and their parents by the use of the word 'identical', when the researchers or health care professionals know they themselves do not mean 'identical' in the usual sense. So why mislead the confused parents?

It is a paradox that, in an age when so much emphasis is placed on the influence of parenting and rearing on the development of all children, we use the word 'identical' for MZ twins to imply that genes are the beginning and end of development, with no other factors involved. Even if MZ twins were genetically identical, this would be terribly wrong. The results of testing MZ twins reared apart show how highly similar they are in ways that we could not ever imagine to be genetically based,[2] but I am not aware that anyone thinks they are 'identical'.

Consider the following examples.

My colleague Dr Louis Keith, (a renowned twin researcher) and his twin brother, Donald, were convinced into their 40s that they were DZ because everyone can see differences, most obviously in depth of skin pigmentation. Multiple blood protein tests at that time showed that they were MZ (which is what everyone but themselves believed). But the whole issue boiled up again in their 60s when they decided to have definitive DNA-based zygosity testing done, using RFLPs and several loci. They turned out to be discordant at one locus, raising again the question of dizygosity.[3] Every one views this difference at a single locus as a post-zygotic mutation, and that most, if not all, MZ twins are genetically discordant, the number of mutations perhaps increasing with age.

A few years ago, I published (with the twins as co-authors) a paper in which twin males had from an early age designated themselves as DZ because they were not completely 'identical'. This had disastrous consequences many years later, when one twin was a living renal transplant donor for the other twin, who had been on immunosuppression therapy (with significant complications) for 15 years before I met the twins for the first time and told them I thought they were MZ. We proved this by formal

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DNA zygosity testing, and the recipient can now sleep at night secure in the knowledge that he won't reject his donated kidney tomorrow if he forgets to take his cytotoxic drugs – from which he has been weaned while maintaining normal renal function. The 15 years of anxiety, chemotherapy and complications had been completely unnecessary.[4] The twins were MZ, but not 'identical'.

Take a close look at the amazing case published in the Lancet.[5] These boys have very marked pigmentary and other physical differences, but they were MC and they have had more DNA tests than any other twins on the planet. They were definitively MZ.

Here is my latest e-mail case. The twins' mother is a nurse, and she knows what MC and MZ mean. The boys were MC, but they have different birthmarks and freckles, so they are not 'identical'. Somewhat against her better judgement, she did check swab DNA sampling and was sent back a DZ result from a highly reputable genetic laboratory. There is no doubt in my mind from the photographs that these twins are MZ, and their placenta says so. But the word 'identical' was used, so now we have to sort it out all over again.

So let us spare twins and their parents the pain and anguish of the word 'identical'. MZ twins are not identical in any way. Many (perhaps most or even all) are not even genetically 'identical'. Parents of MZ twins resort most frequently to the hypothesis that their remarkably similar twins must be of the 'third' or 'polar body' type. I am deeply skeptical that polar body twinning can explain any but an extremely small number of cases, and I myself have never seen a pair. There is only one well-documented pair in the entire literature,[6] and these have not been re-tested in the DNA era – I think they should be. Whenever I visit twins' clubs, I always ask parents to bring photos of their twins if it is past their bedtime. I think I am fairly good at sorting out zygosity, and the way I do it is to hold up a photo and get all the other parents to vote. By then they have learnt that MZ twins are not 'identical' and a majority of parents immediately get the idea and will vote MZ cases as MZ because 'they are too alike to be DZ', which is my criterion. Invariably the index parent is mortified that everyone else finds zygosity diagnosis so easy, although they can do it on other twins. Of course their twins are not 'identical'. Of course they definitely are MZ. We have to teach a 'Gestalt' approach, which simply says that the resemblances are not due to random sorting of genes during the development of two zygotes. They are the result of genetic and non-genetic effects on development of twins derived from one zygote, such that no two humans, even when MZ, will be as 'identical' as two cars coming off the assembly line.

MZ twins absolutely need to know that they are MZ, because of the heavy implications for concordance/discordance for QTL disorders[7] and for transplantation. The declaration of twin rights states that knowledge of zygosity is a birthright.[8] Let us therefore use the correct zygosity terminology. Twins and their parents are perfectly capable of understanding what zygosity means, and that MZ simply means derived from one zygote without any implication whatsoever that the twins will be 'identical' in the accepted sense of that word. To use the words 'identical' and 'fraternal' is probably more detrimental than not telling twins or their parents anything about zygosity – 'it's none of your business', or 'it will become obvious with time', or 'it doesn't matter'. All of us know of twins and families who have been fobbed off with those sayings. Let us tell them the precise truth as we know it. I think it is likely that the majority of twins and their parents throughout the world today are confused and misled because of imprecise terminology, as a result of which their zygosity is actually completely unknown to them. The community (I nearly said fraternity) of twins and their parents should be encouraged to understand that we don't really mean 'identical' when we say 'identical', so let's not say it. That should be perfectly clear.

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## References

1 Machin GA. Some causes of genotypic and phenotypic discordance in monozygotic twin pairs. Am J Med Genet 1996; 61: 216–228.
2 Bouchard TJ, Lykken DT, McGue M et al. Sources of human psychological differences: The Minnesota study of twins reared apart. Science 1990; 250: 223–228.
3 Keith L, Machin G. Zygosity testing. Current status and evolving issues. J Reprod Med 1997; 42: 699–707.
4 St Clair DM, St Clair JB, Swainson CP, Bamforth F, Machin GA. Twin zygosity testing for medical purposes. Am J Med Genet 1998; 77: 412–414.
5 Gingras P. Identical differences. Lancet 1999; 353: 562.
6 Bieber FR, Nance WE, Morton CC et al. Genetic studies of an acardiac monster: Evidence of polar body twinning in man. Science 1981; 213: 775–777.
7 Martin M, Boomsma D, Machin G. A twin-pronged attack on complex traits. Nat Genet 1997; 17: 387–392.
8 Declaration of rights and statement of needs of twins and higher order multiples. Twin Res 1998; 1: 52–55.



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