

RESPONSE to the CRITIQUES of  
Atypical Gender Development – A Review

Three critiques of the article 'Atypical Gender Development – A Review' (hereafter 'the Review') are published together with it. GIRES acceded to the editors demand to waive typical publication procedures, so that the original review, the Journal's reviewers' comments on it, and this response should be published simultaneously. The response to the critiques of the Review appears below. The numbering of the paragraphs in this response is not related to that in the original article.

The Preamble to the Review

1. Kenneth Zucker's interpretation of the 'preamble' is incorrect. He assumes that the description of the Trans group, when it was originally established some twelve years ago, as being concerned with the reform of the International Classification of Diseases (ICD)<sup>1</sup>, applies to GIRES and, perhaps, the whole team. It does not. Neither GIRES nor the other contributors to the Review had the ICD in mind when the article was written. The reviewers have put their own interpretations on our text and, consequently, much energy has been devoted to criticising our supposed motivation for writing this paper.

Zucker's misreading of the text is unfortunate, since it seems to have coloured his interpretation of the paper and his language. His use of words like 'agenda' and 'manifesto' are in themselves 'political' and take the article into realms that were never intended by its contributors. Nevertheless, we have responded to the wider political issues, in the spirit of broadening the discussion.

We suggest the opening of the preamble be understood as follows:

*In 2003, the Gender Identity Research and Education Society (GIRES) ran a small symposium in London, assisted by a Trans Group (founded in 1993 to work for the benefit of people affected by transsexualism). GIRES was awarded additional funding for this project from the King's Fund - an eminent charity providing funds for medical and scientific work.*

Etiology

3. It is, perhaps, not surprising, given the historical emphasis on the psychiatric diagnosis of transsexualism, that the reviewers, two psychiatrists and a psychologist – in contrast to the balanced multidisciplinary team that contributed to the Review - would find it hard to accept that biological ingredients might outweigh psychosocial factors in the development of the condition. It would be fair to say that, in writing the Review, the contributors hoped that biological factors would come to be regarded as making an important contribution to the etiological factors leading to transsexualism. There is acknowledgement in the Review that social factors are certainly also involved in any expression of gender identity, whether typical or atypical.

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<sup>1</sup> The misleading reference to the ICD has been removed from the version of the original article on the GIRES' website.

However, although there is a different emphasis in our paper than the reviewers would favour, we all appear to have elements in common.

4. Friedemann Pfäfflin's first point refers to the great variety of manifestations of transgenderism, and therefore the unlikelihood of an explanation which depends on a single factor: 'constitution, morphology, hormones or psychology'. This seems little different from the Review statement:

*"The etiological pathways leading to this inconsistent development almost certainly vary from individual to individual, so no single route is likely to be identified. Different genetic, hormonal and environmental factors, acting separately or in combination with each other, are likely to be involved in influencing the development of the psychological identification as male or female. Psychosocial factors and cultural mores are likely to impact on outcome"* (Review, Point 44).

5. So, we can all agree that there is no 'uniform somatic disposition'. Pfäfflin's description of the huge variety he sees within his patient group, does not dispel the notion of a biological element in most, or even all, of these cases. Richard Green raises the issue of 'behavioural subgroups' of transsexual people which, he maintains, militates against a 'common developmental pathway'. Of course, 'a common developmental pathway' is also not postulated, or possible, given the immense complexity of the potential interactions of all the following elements: hormones, and hormone receptors (variations of which are numerous within the main subgroups, AR, ER $\alpha$  and ER $\beta$ ), neurons (some of which are now understood to acquire sex-specific properties independently of their hormone environment; Mayer *et al.*, 1998; Dewing *et al.*, 2003; Swaab *et al.*, 2004) and also synapses. Furthermore, a variety of outcomes *should* be expected; transsexual people are no more likely to be uniform in their experience of gender (or other aspects of their psychological development, or their psychosocial interactions with others, or any personal strengths, frailties or other characteristics) than are the non-trans population. The contributors to the Review would agree with Pfäfflin's assessment that in some of the cases of 'regret', which he sees in his practice, 'psychosocial factors' are involved. Landén's research, for instance, pointed strongly to factors such as lack of family support in undermining the potential success of transition (Landén, 1999).
6. However, it is likely that underlying biological factors are also an important factor in many cases of the regret to which Pfäfflin refers (his Point 3). Those whose gender identity hovers near the middle of the gender spectrum, may feel uncomfortable in one role, but not necessarily more comfortable in the other. Yet medical treatment often colludes with society's demands for conformity with one role or the other, so some individuals experiencing gender dysphoria feel compelled to travel further than they need across the gender divide, for fear of being regarded as 'ambivalent' and jeopardising access to treatment altogether. Inevitably, some will complete full transition, including surgery but, having not achieved the comfort they seek in the opposite role, these individuals draw back. Where discomfort in the new role is already being experienced, psychosocial factors may seriously aggravate the situation: the intensity of loss – of family, of employment, of status, of financial ease are, sadly, a frequently acknowledged concomitant of transition. Biology loves variety, but society hates it (Diamond, 2005), so trans people struggle to find a

balance between their very human need to conform, and their profound experience of being different. It's not surprising there are regrets. It is surprising there aren't more, but none of this disproves a biological ingredient.

7. Pfäfflin goes on to say that the role of the central subdivision of the bed nucleus of the stria terminalis (BSTc) is given undue weight. It is true that, in terms of the number of words, more were devoted to the Kruijver research than to other individual studies (Kruijver *et al.*, 2000). This study, and its predecessor (Zhou *et al.* 1995), are the only directly relevant post-mortem brain studies available. In order to understand both their limitations and their strengths, it was felt necessary to cite details of the actual numbers of post-mortem transsexual brains collected, which were, admittedly, small (n=8; controls, n=34), as well as the reasoning for ruling out hormone treatment as a possible cause of changes to the adult BSTc. Green, in his comments on the Review, draws the perplexing conclusion that the divergent development of the BSTc is found to be 'not dependent on pubertal hormones'. It is not clear from where this inference is drawn. It is not tested in the BSTc studies; only hormones in *adulthood* were ruled out (Kruijver *et al.*, 2000; Swaab; Kruijver, 2005). However, it is thought that a follow up study of somatostatin and total neuron-count, as well as somatostatin *in situ* hybridization, during the course of development of the BSTc, might be of interest, in order to determine whether or not the higher circulating androgen levels at prenatal, neonatal and/or pubertal ages might be associated with typical changes in its neuronal cell division, neuronal activity or apoptosis (Kruijver, 2004).
8. We would, perhaps, all agree that the brain studies, *taken in isolation*, do not provide incontrovertible evidence of a link with transsexualism. The Review is criticised for treating correlations as if they were causes, and this is particularly applied to the BSTc. It is not accepted that the Review does treat correlations in that way. The extract quoted at the beginning of this response (Point 4) clearly indicates an understanding that there are a number of pathways, and a number of triggers, varying greatly from individual to individual. The BSTc is not postulated as *the cause*, or even *a cause*, but rather as *a possible link* in an etiological pathway, since it corroborates the involvement of a brain difference, which is already inferred from other studies mentioned in the Review.
9. What the Zhou and Kruijver brain studies demonstrate undeniably, however, is that parts of the brain, known to be sex-dimorphic, show neural differentiation, which is both internally inconsistent (i.e., within the brain) and is in opposition to genital and gonadal characteristics. That is not only unarguable, it is also to be expected. Since the latter aspects of sex-differentiation - genitalia and gonads - are somewhat prone to atypical differentiation, it is highly likely that there will be a certain amount of sex-variability in the brain also. There would have to be some exceptional reason for assuming that the brain was immune from such variability in its neural development. There is also evidence from animal research that the nervous system is even more sensitive to hormonal influences than are somatic tissues (Goy *et al.* 1988). It still begs the question, of course, as to whether this is connected to the development of transsexualism. At the moment, until research proves that it isn't, it seems statistically likely that it is, since coincidentally the 8 trans brains collected, as well as the 34 controls, met the paradigm. And, if not this locus, as the Review suggests, "*possibly other, as yet unidentified, loci*"(Review, Point 44).

10. As suggested above, even without the BSTc studies, it would be possible to infer an atypical brain ingredient in the development of transsexualism. If the postulated innate predisposition exists (Coolidge *et al.* 2002; Kruijver *et al.*, 2000; Gooren, 1999; Zhou *et al.*, 1995; Diamond and Sigmundson, 1997) it necessarily resides in the brain (no other organ can house a psychological identification). The co-occurrences in families and the twin studies indicate, as is hypothesised, that there is, *in some cases*, an inherited factor, therefore, genes and the central nervous system (CNS) are inevitably engaged.
11. In relation to prenatal androgen exposure in individuals with Congenital Adrenal Hyperplasia (CAH) and a complement of 46 XX chromosomes, who are raised female, Zucker asks (his Point 24) "how come their gender identity is not grossly masculinised?" Perhaps, sometimes, it *is*. This might account for those XX individuals with CAH (referred to under Point 22 by Zucker) who are raised male and continue to identify as such. Presumably they were raised male because their genitalia were severely virilised. Why would one assume that their brains were totally immune from this high level of masculinisation? Regarding the majority of the XX individuals with CAH, who are raised female and continue to identify as such, might one not better ask, 'how come their behaviour is masculinised at all (which it is), and how come a significantly raised incidence of transsexualism (albeit still a small number) is found in these individuals, despite female rearing and female phenotype (sometimes surgically 'corrected')? The risk of developing transsexualism is raised by a factor of between 300 and 1,000, in such individuals (incidence of transsexualism in XX, CAH estimated at between 1% - 3%, Hines, 2004, compared with that of females in the general population, which is estimated to be 0.003%, extrapolating from Wilson *et al.* 1999).
12. With reference to the cloacal exstrophy studies by Reiner, Green accepts that there may be an 'innate' identity as male 'for persons with the XY karyotype and normal prenatal androgen' but, he argues, 'this does not demonstrate that a cross-sex identity is also innate'. This is not how the cloacal exstrophy studies are used in the Review. Rather, what they show, taken in conjunction with other evidence, is that:
 

*"gender identity often resolves independently of genital appearance, even when that appearance and the assigned identity is enhanced by medical and social interventions. It is, therefore, postulated that the brain is often the stronger factor in determining gender"* (Review, Point 24).
13. It would seem that Green is agreeing that karyotype and pre-natal androgens are implicated in the development of the brain, and that this, in turn, may impact on gender identity in the general population. So, it's good to see that we can agree on that possibility. The implications of this are, of course, that, typically, gender identity will be consistent with other sex characteristics. Logically, however, the converse of this, is that any *atypical* genetic and/or hormonal input could, potentially, give rise to a gender identity which is also atypical and not necessarily consistent with the phenotype (whether 'corrected' or not).
14. Both Green and Zucker refer to recent reviews of individuals with 5 $\alpha$ -RD and 17 $\beta$ -HSD conditions. Green indicates that a significant proportion of these individuals, having been assigned as females in contradiction to their XY chromosomes, nonetheless, 'continue living as women'. Green implies

that, the fact that these individuals do not revert to the gender role which is consistent with their karyotype, but rather continue in the gender in which they were reared, reinforces the 'rearing' argument for determining gender identity. But the proportions cited by Green are that one third of  $5\alpha$ -RD individuals, and half of  $17\beta$ -HSD *don't* change. So, *two* thirds of  $5\alpha$ -RD individuals, and half of  $17\beta$ -HSD *do*. The point is endorsed in the surveys of  $5\alpha$ -RD cases (n = 90), reared as females, in 23 countries, 64 individuals (71%) reverted to the male sex (Bosinski, 2005). This represents an increased risk of the emergence of a male gender identity by a factor of 5,300 among  $5\alpha$ -RD individuals, and a factor of 3,700 among  $17\beta$ -HSD individuals, compared to the general population. Quite enough to make the point at issue, that gender of rearing doesn't *always* overcome innate gender identity.

In addition, observations such as those of Sobel *et al.* (2004) should be taken into account in all cases of genotypical males raised female. 'Some individuals may desire to continue to live as females; whether they have a truly female gender identity or whether they are inhibited by social and family pressures from revealing their true gender may not be easily discernible'. Another factor is that the interviews which evaluate gender satisfaction are often couched in terms that are unlikely to elicit information about gender discomfort.

15. Zucker points to the Diamond and Watson (2004) article as an example of biased selectivity in reporting, since the pAIS cases discussed in that paper, and cited in the Review, were not clinically diagnosed. He says, 'it appears that the diagnosis was made by the patient'. Zucker is incorrect, as note 1 of the cited paper states, 'All study participants had confirmed diagnosis of cAIS or pAIS...' These diagnoses were confirmed by genital fibroblast identification tests or by DNA. Zucker further complains that many references have been omitted from the discussions about outcomes in conditions of  $5\alpha$ -RD and  $17\beta$ -HSD. It is true that the Review list is not exhaustive, although adding more of these (and this also applies to the other conditions mentioned, would add little to the point which is simply to indicate that the gender of rearing does not *guarantee* a consistent gender identity, so another ingredient must be at work. The Review does, in fact, cite a study that Zucker believes we have omitted: Wilson, Griffith & Russell, 1993. The sources, relating to this point, cited in the Review are: Imperato-McGinley *et al.*, 1974; Imperato-McGinley *et al.*, 1979a; Hurtig, 1992; Wilson *et al.* 1993; Imperato-McGinley *et al.*, 1979b; Rösler & Kohn, 1983; Kohn *et al.*, 1985; Rösler, 1992; Sobel and Imperato-McGinley, 2004), but undoubtedly there are many more studies that we could have cited. Zucker further complains that the Review doesn't mention the  $5\alpha$ -RD sister in the Hurtig (1992) study, who continued to identify as female. The same reasoning applies here as elsewhere in the Review. The question is not 'why is this child's gender identity consistent with her gender of rearing', the question is, 'why is her sister's *not*', considering that they were reared in essentially the same way. Zucker comments that some reviews of earlier studies indicating gender change in some of the intersexed groups 'reach a different conclusion about its commonness'. But, no matter how uncommon, the fact remains that these groups provide numbers of examples of individuals in whom an apparently innate gender identification has held sway over socialisation.

16. Criticism was expressed for using information relating to intersexed persons when discussing transsexualism in the Review. It is probably,

therefore, worth clarifying the rationale for doing so, and for the inclusion of other material, John/Joan and cloacal exstrophy, for instance. All these cases are relevant, and discussed, for several reasons: firstly, to demonstrate the extremely wide and varied nature of sex differentiation - not everyone sits comfortably at one end of the sex spectrum or the other but may have mixed characteristics; secondly, these cases demonstrate that, powerful though phenotype (whether engineered or not) and gender of rearing are, in influencing the development of gender identity, they do not always triumph; thirdly, many of the cases indicate that an unusual level of androgens, at the fetal stage, is certainly implicated in variations in sex-differentiation; fourthly, unusual hormone levels, arising for whatever reason, are implicated, in some individuals, in the development of a brain sex development which is inconsistent with other sex characteristics, and this, in turn, may be a factor in the development of gender identity. In light of the above reasoning, it is plausible to regard transsexualism as part of this wide variation. Some researchers, therefore, consider transsexualism to be a form of intersexuality (Diamond, 1999; Gooren, 1999; Zhou *et. al*, 1995, Kruijver *et al*. 2000; see also Point 31 of this response).

17. The Review does not suggest that any innate predisposition *cannot* be overcome in a proportion of cases, only that there is always a risk that the predisposition will not succumb to socialisation, and manifestly *hasn't* succumbed, in a number of cases. The proportion of those who choose not to transition is also hard to determine with accuracy, since many individuals transition later in life, years after interviews have recorded an apparent stability in the assigned gender.
18. Green states that the Review doesn't cite the studies on DES which contradict its potential influence on gender development. This is true, although we do, of course, say that it remains "*an unproven hypothesis*" (Review, Point 42), and we make it clear that the hypothesis is largely based on self-reports. Two of the studies Green suggests we should have included in the Review are fairly old, 1973 and 1980, when arguably fewer transsexual people were admitting their condition, or seeking treatment; more attention was still being given to daughters of mothers prescribed DES. It is interesting, however, that Green's findings in the 1973 paper indicated 'more masculine boyhoods than other groups'. This could, perhaps, be interpreted as the result of macho endeavours, and reluctance to report gender variance, which emerge from what Zucker regards as 'biased' biographical accounts (see his Point 6).
19. The published Meyer-Bahlburg (1997) study to which Green refers, deals with sexual orientation rather than gender dysphoria. For what it's worth, and in the interests of furthering the discussion, the results of the self-reports (which we didn't include in the Review because of the acknowledged weaknesses of methodology) were from a survey conducted in 2002, of 63 DES sons, who were asked to self-define. They responded as follows:

23	36.5%	transsexual individuals
11	17%	straight males
9	14.3%	transgendered individuals
6	9.5%	gay males
6	9.5%	androgynous individuals
2	3.1%	intersex individuals
2	3.1%	bisexual males
2	3.1%	other

1	1.5%	female
1	1.5%	eunuch

As hearsay and circumstantial evidence continues to accumulate, there are researchers who believe that the DES connection is a possibility well worth pursuing, prompting comments such as McLachlan's in 2001, that "a good number of men subjected to DES have switched their gender role from man to woman".

20. The Review is also criticised for explaining that one of the reasons that there has been some modification of the previous views about early genital surgery is the voice of those who are unhappy with their treatment – the Intersex Society of North America. Zucker questions 'the extent to which they are representative...' However, the Review (Point 26) is careful to say that *many* are unhappy with their surgery, and "*some but not all are uncomfortable with the gender role...*" There is no attempt here, to say that discontent is universal among those operated on as infants, but for those who cannot identify in the gender assigned, the results of such treatment may be regarded as disastrous, *and* no matter how few they may be, these individuals are responding to an innate sense of themselves. There is now a growing recognition that these early genital surgeries may be problematic for a significant number of individuals (Beh and Diamond, 2000; Ramecroft, 2001; Creighton, S., 2001; ISNA).
21. The failure of socialisation to provide *infallibly* consistent outcomes, and the failure of conventional psychiatric treatment to 'cure' the persistent experience of transsexualism (Green, 1999), the known impact of hormones on brain development and structure, and a picture of possible, overlapping, inter-related biological factors builds up. It is when the brain studies are considered in the context of other biological pointers, that they support the paradigm that the neurobiology of the brain is an important element in the development of transsexualism (Zhou *et al.*, 1995; Kruijver *et al.*, 2000).
22. Green comments, with respect to his own study on 'non-right-handedness' amongst trans men and trans women, that more transsexual people are right-handed than left; also that more XXY individuals identify as male than female, that the majority of XX CAH individuals identify as female, that most twins do not experience transsexualism etc. But this does nothing to undermine the view that there is a biological element in the development of transsexualism. The current understanding is that there is a raised incidence of sinistrality in transsexual people, and a raised incidence of gender dysphoria in the other groups mentioned, which defies the logic of placing all reliance on conformity of genitalia, gender of rearing, or other psychosocial factors as the ultimate determining causal factors of gender identity.
23. The question of 'handedness' provides a useful analogy. Transsexual people are in a similar position to left-handed people who, even well into the 20<sup>th</sup> century, were forced to write with their left hands tied behind their backs. Left-handedness was regarded as being, literally, sinister. Yet everyone now accepts that it is both hard-wired and benign, and society has abandoned its attempts at enforcing conformity. Just like those experiencing a gender identity which feels inconsistent with the gender role expectations of society, some left-handers adapted reasonably well to society's demands; some adapted with difficulty; and some continued to use their left hands when no-one was looking! A day may come when

society abandons the notion of gender conformity also, but today, in gender terms, society requires people experiencing gender dysphoria to develop with one hand tied behind their backs. They try to adapt to the conventional norms; some succeed in adapting; some don't; some compromise, some alter their gender role only when no-one is looking. Some, abandon the struggle to maintain the new role, and revert to their original presentation. Individual responses, and the social situations to which they respond, are infinitely varied.

24. So, the argument is not that psychosocial factors are unimportant, indeed, it is acknowledged in the Review, "*that one's upbringing and genital appearance .... will have a significant impact on gender expression*" (Review, Point 29). John Money, in his later years, came to see that "there is no one cause of a gender role ... Nature alone is not responsible, nor is nurture, alone. They work together, hand in glove" (1994). Zucker refers to the twin studies by Iervolino and others which provide evidence for 'shared environmental influences on gender role development...' Again the Review acknowledges the impact of environment on gender *role*. Gender identity, however, is a different matter, and the question remains, why do genital appearance and consistent gender of rearing not *guarantee* outcomes. And if the reviewers postulate that an innate biological predisposition is *not* present, what evidence is there that some *non*-biological factors inform, sometimes even very young children, that they are, emphatically, what the world tells them they are not? Zucker suggests, perhaps rather unwisely, that "autobiographical material is obviously biased". Possibly, but this material may also be factual, enlightening, and important. We should all, perhaps, be listening more, not less.
25. The nexus of the Review's position, is that a natural variation in development is sufficient, *in some individuals*, to override physical appearance and gender of rearing. Clearly, genitalia are not the only reality, and certainly not the most important reality for individuals experiencing transsexualism. However, the Review does not deny psychological influences; indeed, it supports the view that 'rearing' which is inevitably influenced by cultural norms and mores, has a huge impact on outcomes. Yet, the stronger that the element of rearing is demonstrated to be in the development of gender identity, the more amazing it is, that its effects are not invariable nor universal.
26. Societies, varied though these are, provide the sounding board against which we all measure our relative comfort or discomfort as men and women.

#### Advantages and Disadvantages of Biology

27. The commentators on the Review speculate about its purpose and they question the 'usefulness' of involving biology in support of human rights generally, or of better medical treatment. Here, we are already treading in areas that go beyond the remit, and beyond the text, of the Review, but as the issues are raised, and in the interests of completeness, we will deal with them.

Firstly, we all agree, as is clearly stated in the Review that "*it is imperative to emphasise that attention to the needs of trans people should be extended on the basis of human rights, justice and equality. Medical and*



*scientific findings are often amended and clarified, but the right of individuals to appropriate care and respect remains” (Review, Point 45).*

28. However, Pfäfflin seems to be indicating that by discussing the biological aspects of transsexualism, our article might actually be damaging to people affected by transsexualism. He comments that biological explanations can be used against individuals, as well as in favour of them. But the same is true of psychiatric explanations, arguably, more so. Rosenhan found that a psychiatric diagnosis was difficult to shake off, even when totally misplaced; also, it significantly and adversely affected attitudes towards those so diagnosed, even among the clinicians responsible for their treatment (Rosenhan, 1973). There are, undoubtedly, sensitive and compassionate clinicians, who treat patients with respect, but this is far from being universal, and many people seeking treatment for gender dysphoria, complain of the disempowerment and dismissive attitudes of clinicians. There must inevitably be a reluctance to allow patients, who are regarded as psychiatrically compromised (entirely on the basis that they experience such gender dysphoria), a major role in the decision-making process in their own treatment. The attitudes of clinicians may be patronising, at best, punitive, at worst. There is also the negative impact on the funding of treatment by insurance companies and healthcare commissioners who may regard the process of transition to be a lifestyle choice, and surgery, to be purely ‘cosmetic’. In the United States, the diagnosis of Gender Dysphoria, as it is currently understood, can still be a reason for depriving individuals of medical and health insurance.
29. In contrast, the ‘Katia’ case in Madrid, provided a favourable outcome for a person who had transitioned to live as a woman, entirely on the basis that the Court found that she had an intersex condition, thus recognising the somatic nature of her transsexualism. Her right to publicly-funded reassignment surgery followed from that finding. Previously, such surgical correction was only available for other intersex conditions and was denied to transsexual people, specifically, because their diagnosis was psychological rather than somatic; their surgery was, therefore, not deemed to be ‘corrective’ (Katia, 2004).
30. It is also the case that, in the UK, the court case which ensures treatment for transsexual people (Auld LJ, North West Lancashire v A, D & G, 1999) rules out, unequivocally, the ‘human rights’ argument. The lawyers were criticised by all the judges involved for even having raised it. Therefore, in order to secure parity with other medical conditions when funding for treatment is being sought, other arguments have to be deployed. Many of those who make funding decisions in the UK – these are a mix of clinicians and lay people – continue to proffer the ‘lifestyle choice’ and ‘cosmetic surgery’ arguments, and not surprisingly, transsexualism is therefore often accorded extremely low priority in comparison with more supposedly ‘deserving’ conditions.
31. Furthermore, as Pfäfflin implies (his Point 5), treatment philosophies and protocols are apt to be predicated on clinicians’ understanding of the diagnoses and causes of any condition (see also, Cohen-Kettenis and Pfäfflin, 2003). So, it is surely right that additional potential ingredients in the etiology of transsexualism be more widely understood. Also, although it is agreed that the science is far from complete and not necessarily legally persuasive on its own, it has had a significant role to play in a number of court cases, for instance, Judge Chisholm’s findings in the

Re. Kevin case in Australia. Chisholm wisely comments that the argument in favour of "brain sex" does not derive entirely from the two studies, Zhou and Kruijver, but a wealth of other information about transsexualism. He mentions, in particular, 'the evidence about the development and experiences of transsexual individuals, and others with atypical sex-related characteristics'. Chisholm finds that the characteristics of those affected by transsexualism 'are as much "biological" as those thought of as inter-sex'. His findings successfully undermined the famous 1970 Corbett v Corbett case in the UK, which had determined that a person with XY chromosomes, male genitalia and gonads was, unalterably, a man. The narrow biological understanding in this case has, inevitably, led to contrary biological evidence being introduced into the court arena. Hence, a more up-to-date scientific interpretation has been 'prayed in aid' in cases such as Gardiner, (2001), Heilig (2003), Kantaras (2003), and Bellinger (2001). In the latter case, Dame Elizabeth Butler-Sloss, recognised in her general conclusions that 'There is, in informed medical circles, a growing momentum for recognition of transsexuals (sic) for every purpose and in a manner similar to those who are inter-sexed'. Pfäfflin raises the issue of the Gender Recognition Act in the UK, which was resolved, quite rightly, on the basis of human rights. However, the Chair of the Parliamentary Forum for Transsexualism ensured that a brief account of potential biological factors was circulated, in hard copy, to members of the committee set up to examine the draft legislation, and electronically, to all Members of Parliament, before they finally voted on the Bill. This was judged by the Chair of the Forum to be valuable in shaping attitudes of those whose job it was to pass the Bill into law.

32. Issues of biology were raised in both the House of Commons and the House of Lords. In the latter venue, Lord Winston, a renowned specialist in reproductive medicine confronted the Evangelical Christian argument with the following:

*"Good evidence has emerged from Professor Waters of Monash University in Australia... that suggests that some people who become transsexuals (sic) later in life have been exposed to an abnormal surge of either male or female hormones during pregnancy"* (Hansard).

33. This statement, the probity of which some might challenge, is used here only to demonstrate the perceived value of the biological viewpoint in winning the hearts and minds of those who had to vote on the human-rights-driven Gender Recognition Act (2004). This perception also emerged from Landén's doctoral research, undertaken in Sweden in the 1990s, which found that attitudes towards transsexualism were more liberal where the condition was understood to be biological rather than psychological in origin (Landén, 1999).
34. Nevertheless, it is accepted that potential disadvantages as well as benefits may flow from an understanding of the scientific research in this area. However, for better or for worse, people experiencing transsexualism are entitled to knowledge and recognition of whatever evidence emerges. It would be immensely patronising to deny them, and others, knowledge of such research and its implications, merely on the basis that it *could* be used against them. Even where no benefit accrues (which is certainly not the case here) human beings are imbued with intense curiosity; they pursue knowledge in a bid to understand themselves and their world. **The need to know goes beyond 'usefulness'**. The case of transsexualism is no exception. Importantly,

too, whatever is learnt about the development of gender identity through studies related to gender variance, has implications for the non-gender-variant population; we learn something about the development of gender identity in all of us.

35. The reviewers raise the issue of the history of homosexuality and its related science. As with transsexualism, many different studies, some contradictory, Le Vay v Byne for instance, have been discussed over the years. Views are still far from universal on the origins of homosexuality, but gradually the notion has gained ground, that homosexuality is, indeed, more the result of biology than a life-style choice, and that upbringing has little relevance (Wilson and Rahman, 2005). Green comments on the variegated history of 'cause' in relation to homosexuality, saying that it was fortunate that 'all gay eggs weren't in one basket'. The implication is that the Review makes the error of over-reliance on brain biology, specifically the BSTc (the one basket) in relation to gender dysphoria. We would argue that the Review does exactly the opposite. We offer a range of research indicating possible biological etiologies, *against* the 'all eggs in one basket' diagnosis of mental illness/psychiatric disorder. This diagnosis has, for a long time, precluded other interpretations of the wider evidence. It's time that an additional basket of eggs was given due consideration.
36. Zucker offers a rather convoluted view in his 'summary'. He accepts that 'biological causation' has been tried with homosexuality 'with some success'. However, despite this 'success', he then argues that the 'liberal argument' is 'flawed' (citing Halley on sexual orientation) and, presumably, he therefore believes that this argument should not be available to people experiencing transsexualism. To maintain that a 'successful' argument should not be used, seems peculiarly obtuse. It is important to emphasise, too, that these people, like gay and lesbian people, seek, not merely to be *tolerated*, which, we would agree, should be achievable via the 'human rights' route, but they wish for the complete *acceptance* which derives from a real understanding of the condition. The benefits of a better understanding of homosexuality is highlighted by Ben Summerskill, the chief executive of "Stonewall", the most powerful lobby group for gay and lesbian people in the UK. In the newspaper, the "Independent on Sunday", July 13th 2005, Mr Summerskill welcomed the recently-published Wilson and Rahman book, "Born Gay", which emphasises the biological ingredients in the origins of homosexuality. He commented that the book provides 'welcome evidence' that makes 'discrimination against gay people untenable'. The conclusion, rightly or wrongly, that there are perceived benefits to a biological explanation is, therefore, inescapable (see also Ernulf *et al.* 1989). The contributors to the Review do not suggest that present scientific knowledge in respect of transsexualism is complete or conclusive, but in the same way as for homosexuality, it enhances the human rights argument, and may be used in conjunction with it, in combating discrimination and promoting genuine acceptance of those experiencing transsexualism. The argument offered by Zucker is perhaps, 'flawed' in itself and is, in any case, irrelevant in respect of the text of the Review.
37. Nonetheless, it is disingenuous of the Review's critics to suggest that a knowledge of what science has to offer has no potential benefits, when it clearly has been an important element in developing positive attitudes in the field of diversity.

### Non-substantive points

38. The reviewers raised some non-substantive points and others that are tangential to the main arguments. We suggested dealing with these matters, in the usual way, prior to publication, but the editors declined this offer. In view of the time constraints to answer all three commentaries the following responses are not exhaustive. These are discussed below.
39. Zucker mentions that, at Point 2 of the Review, we do not refer to 'psychological treatment'. In this paragraph we are discussing 'the typical triadic therapy' (as outlined in the Harry Benjamin International Gender Dysphoria Association's Standards of Care (HBIGDA, SoC, 2001, p 8); this does not include psychological treatment. In fact, the HBIGDA guidelines make it clear that psychotherapy is not necessary for all service-users experiencing transsexualism. However, the role of such treatment is covered at Point 3 of the Review, but Zucker does not mention this. The actual wording is:
- "It is recommended that psychotherapeutic support be offered in conjunction with all the procedures outlined above, to facilitate adaptation to the appropriate gender role and address any associated emotional difficulties, especially in regard to family and social relationships"* (Review, Point 3)
40. Zucker also asks (rather facetiously) if one should infer that 'a three year old child diagnosed with GID should be treated by the realignment of the phenotype...', and he also proposes that when we quote, Green at Point 4 of the Review, we should make it clear he was referring to adults. But this is already clarified at Point 2, the text indicates that we are speaking of *those experiencing transsexualism, the extreme form of the condition*" Zucker then acknowledges that we go on to discuss child/adolescent issues separately, at Point 5 of the Review. So it's hard to see the justification for his complaint.
41. Zucker's assertion, that the Review at Point 7 'likely' refers only to those who later transition from the male to the female role, is not correct. Many individuals who transition from female to male, also feel pressured to conform to stereotypical behaviours as is described in the Kotula (2000) stories which Zucker regards as 'obscure' He comments that the Review, at this point, is inconsistent with histories of those (still referring presumably male to female individuals) whose pathway to transsexualism includes homosexuality. Yet, the pathway outlined in the Review seems to be applicable to those expressing cross-sex behaviours regardless of whether they live as homosexual men or heterosexual men before transitioning to live as women. Indeed, much the same thing applies to those who continue live as homosexual men in adulthood, without experiencing gender dysphoria. The Review refers to "falling in love, the wish to have a long term partner", "the desire to have children", "embarking on family life" in the forlorn hope of a 'cure', experiencing "stress occasioned by their efforts to suppress cross-gender behaviours".
42. Wilson and Rahman, 2005 identify exactly those behaviours and emotions in homosexual people:

*"More subtle pressures to conform with heterosexual norms sometimes push gay men and lesbians towards having sex with opposite-sex partners contrary to their real feelings. Some find it easier just to go through the motions of heterosexual behaviour than to deal with the social stigma of being called gay. Also, homosexual people are not without parental urges....."*

43. The Review is found lacking by Zucker because it does not address the issue of a possible correlation with childhood abuse. He mentions Devor's study on female to male transsexual individuals. No doubt, had this study been referred to in the Review, it would have been criticised because, as Zucker highlights, himself, the study 'lacked comparison groups'. This significantly diminishes its usefulness. The recent study to which he refers, Gehring and Knudson (2005), also has no control groups, and the authors find that the abusive events were 'the result of adolescents satisfying their curiosity about the gender of the transsexual (sic) rather than for their own sexual gratification'. Clearly, in this study cited by Zucker, the unwanted behaviours arose as a result of the gender variant condition, rather than the reverse and cannot, therefore, be considered in any shape or form, to be a likely part of its etiology. The authors conclude that "the results...do not support any notion that childhood trauma is associated with neither (sic) the formation of transsexualism nor (sic) an issue that seems salient for therapeutic intervention per se...." Reference to this study would have taken the Review up a blind alley.
44. Zucker says that the data on the frequency of gender dysphoria among certain atypical chromosome configurations is unclear (Review, Point 18). We agree that epidemiological data are not available. However, Wiler et al. (1979) found two Klinefelter individuals among nine candidates referred for genital surgery. Several investigators, aside from Seifert (1995) - who is cited in the Review - report Klinefelter individuals who had aspects of gender dysphoria or who actually transitioned to live as women (Baker and Stoller, 1968; Parks, 1977; Diamond and Watson, 2004). Waltzer and Hurwitz (1970) concluded that all their Klinefelter patients judged their own personalities to be dual male and female. These reports do not provide quantifiable evidence, but in view of the rarity of gender variance, it does seem justifiable to infer an enhanced risk of gender dysphoria in Klinefelter and related karyotypes. The evidence of undervirilisation in many of these individuals is more easily established, which also lends support to the perception, among some clinicians, of a raised incidence of gender dysphoria among those with a Klinefelter condition.
45. Green raises the issue of the John/Joan case, and its counterpart which, he believes, the Review does not treat neutrally. However, the reversion of Joan to John, in adolescence, is not unique in the literature. A six month old boy who suffered a traumatic loss of his penis, and was reassigned as female in 1981, refused hormone medication and requested reassignment as a boy in adolescence (Ochoa, 1998). Interestingly, this Ochoa study (n=7, 6 raised male) gives rise to the comment from the author, that 'sex reassignment will not be considered in future in patients with amputation of the penis or emasculation'. It is acknowledged that the decision to opt instead for penile repair is also influenced by the improvement in the relevant surgical techniques.
46. Zucker cites Chung *et al.* (2002) and seems to be indicating that the Review missed this information, but it is clearly mentioned at Review Point 34. However, it is, of course, highly desirable, as Zucker indicates with

regard to Points 33-36 of the Review, that replication of the existing brain studies and/or further research into other loci, be carried out.

47. Undoubtedly, at Point 37 of the Review, there are other studies that could have been considered with regard to ruling in, or ruling out, possible factors impacting on the fetal hormone milieu. Zucker says, 'no study has examined the role of prenatal stress on gender identity differentiation'. We can agree about that and we mentioned none. At Point 37 the Review talks about the correlation between sex-differentiation (rather than gender identity) and hormone milieu. We refer to any factors that *may* contribute to an altered hormone environment, which *might* include, inter alia 'stress'. The Kaiser (2003) article which we cited in the Review, has been followed by another study which concludes that 'prenatal stress affects the offspring in a sex-specific and sex-reversed way' in non-human mammals (Kaiser, 2005; see also Charmandari *et al.*, 2003). It remains a possibility that this could be linked to unusual gender development in humans, but it is one that has not been tested so far. It deserved its brief mention, in the Review, as another avenue to explore.
48. We requested that Green be alerted to what appears to be his misreading at Point 35 of the text. He refers to what he regards as an error in the Review, which resulted in his comment, 'with 19 signatories, someone ought to have spotted it'. He seems to assume that two sentences at that Point describe one individual. In fact, each sentence describes a different individual. All 19 signatories and the other reviewers read it as such. We offered to clarify the text but we were not allowed to make the following suggested amendment:  
  
*"A high, male neuron number was found in the BSTc of the female to male trans individual, whereas an 83 year old male to female individual, who had identified strongly throughout life as female in contradiction to both karyotype and phenotype, and who had undergone no feminising treatment of any kind, had a BSTc fully in the female range"* (Review, Point 35).
49. The Review refers to the Dewing *et al.* (2003) research indicating a direct genetic effect on the sex-differentiation of the brain, in mice, which precedes fetal gonadal input. Green's comment 'beware the distinctions of mice and men', appears gratuitous, since the Review includes the comment that these "*direct genetic effects on brain differentiation... have not yet been demonstrated in humans*" (Review, Point 30). The likelihood of such direct genetic effects, however, is supported by the findings that the two Y chromosomal genes, SRY and ZFY, that are involved in sex-determination of the gonads, are transcribed in the hypothalamus, and frontal and temporal cortex of the adult male human brains. (Mayer *et al.*, 1998, mentioned at Point 12 of the Review).
50. Despite the difference in balance between the views of the contributors to the GIRES' Review, and the three reviewers from the IJT, perhaps we would all agree that science and biology will, undoubtedly, continue to form a part of ongoing discussion in relation to gender dysphoria and transsexualism. There cannot be any field of human development, where limiting the dissemination of knowledge is helpful, or tenable.

References:

- Auld, LJ, North West Lancashire Health Authority v A, D, & G, QBC 1999/0226/4;0228/4; 0230/4
- Baker, H.J., Stoller, R.J. (1968). Can a Biological Force Contribute to Gender Identity? *American Journal of Psychiatry* **124**(12),1653-1658.
- Beh, H.G. & Diamond, M. (2000). An Emerging Ethical and Medical Dilemma: Should Physicians Perform Sex Assignment Surgery in Infants with Ambiguous Genitalia? *Michigan Journal of Gender and Law* **7**(Winter), 1-63.
- Bosinski, H. A.G.,. (2005). Psychosexuelle Probleme bei Intersex-Syndromen, *Sexuologie* **12** (1/2) 31-59.
- Butler-Sloss, E (2001) in *Bellinger v Bellinger*, UK, No B1/2000/3493, neutral citation no: [2001] EWCA Civ 1140.
- Charmandari, E., Kino T., Souvatzoglou E., Chrousos, GP. (2003) Pediatric Stress: Hormonal Mediators and Human Development. *Journal Hormone Research*, **59**(4), 161-179.
- Chung, W.C.J., De Vries, G.J., Swaab, D. (2002). Sex Differentiation of the Bed Nucleus of the Stria Terminalis in Humans May Extend into Adulthood. *Journal of Neuroscience* **22**(3),1027-1033.
- Cohen-Kettenis, P.T.and Pfäfflin, F. (2003). Transgenderism and Intersexuality in Childhood and Adolescence: Making Choices. Sage Publications, London.
- Coolidge, F.L., Theda, L.L., and Young, S.E. (2002). The Heritability of Gender Identity Disorder in a Child and Adolescent Sample. *Behavior Genetics* **32**, 251-257.
- Corbett v Corbett (otherwise Ashley) (1971). P.83(p.D.A.D) 2 All E.R.1 33,44 (p1970) Validity depended on whether or not the respondent was a woman. The respondent, being a biological male from birth, the so-called marriage was void. Consummation not possible as intercourse using the artificially constructed cavity could never constitute true intercourse. Interestingly, intersex, specifically Klinefelter syndrome, was considered by Judge Ormerod, as the respondent was 'partially underdeveloped', but it was ruled out.
- Creighton, S. (2001). Surgery for Intersex. *Journal of The Royal Society of Medicine* **94**, 218-220.
- Dewing, P., Shi, T., Horvath, S., Vilain, E. (2003) Sexually dimorphic gene expression in mouse brain precedes gonadal differentiation. *Molecular Brain Research* **118**, 82-90.
- Diamond (2005) Middle Sex, Horizon, BBC, UK.
- Diamond, M. and Sigmundson, H.K. (1997). Sex Reassignment at Birth. Long Term Review and Clinical Implications. *Archives of Pediatrics and Adolescent Medicine* **151**(March), 298-304.
- Diamond, M., Watson, L.A. (2004). Androgen Insensitivity Syndrome and Klinefelter's Syndrome. In *Child and Adolescent Psychiatric Clinics of North America (Sex and Gender)*. Milton Diamond and Alayne Yates (editors); W.B. Saunders, Philadelphia 13, 623-640.
- Ernulf, K Innala, S., and Whitam, F. (1989). Biological Explanation, Psychological Explanation, and Tolerance of Homosexuals: A Cross-National Analysis of Beliefs and Attitudes. *Psych. Rep.* 1003-1010.
- Gardiner, re Estate of (2001) USA, 29 Kan App, 2d 92, 22 P. 3d 1086, Kan. App., May 11, succeeded based on current medical science. Lost on Appeal March 2002: marriage is between a male and a female.
- Gooren, L.J.G. (1999). Cited in *Bellinger v Bellinger*, Court of Appeal para **32**, Judgement, 2001, TLR 22-11-2000.
- Goy, R.W., Bercovitch, F.B., McBair, M.C. (1988). Behavioral Masculinization is Independent of Genital Masculinization in Prenatally Androgenized Female Rhesus Macaques. *Hormones and Behavior***22**,552-571.)
- Green, R. (1999) Cited in *Bellinger v Bellinger*, Court of Appeal para 32, Judgment, 2001,TLR 22-11- 2000.
- Heilig, R W. (2003). USA, 372 Md. 692,816 A 2d 68, Md., Feb 11. Succeeded based on current medical science
- Hines, M. (2004a). *Brain Gender*, New York, Oxford University Press
- ISNA, <http://www.isna.org/>, Bodies Like Ours [www.BodiesLikeOurs.org](http://www.BodiesLikeOurs.org) and A Kindred Spirit <<http://www.kindredspiritleakeside.homestead.com/Links.html>
- ICD-10 (1993). International Classification of Diseases 10, World Health Organisation, Switzerland.

- Kantaros, (2003). USA No. 98-5375CA (Fla. Cir. Ct Pasco Co. Feb 21. Trial based on Current medical science (gender reassignment surgery not determinative)
- Katia, (2004) August - Spain  
The Social Services Division of the Appeals Court of Madrid ruled against the Madrid Institute of Health (IMSALUD) and for the first time in Spain made health services responsible for funding sex reassignment surgery involving vaginoplasty.
- The facts date back to March of 2000, when "Katia" reported to the hospital in Madrid to initiate the sex reassignment procedure. After several consultations, analyses and other tests..., she requested vaginoplasty at a private clinic which was part of the public health system, at which point the IMSALUD replied that this surgery was not covered except in cases of pathological intersex conditions.
- The Court accepted as proven that "Katia" presented with permanent signs of belonging to the female gender. ...and was "profoundly affected with an intersex condition, and that the guidelines require that sex reassignment surgery be paid by Social Security" when correcting intersex conditions. The Court determined that this was the condition which Katia had. Previous cases in Spain had failed, specifically, because the transsexual individuals concerned were diagnosed with a gender identity problem, not an intersex condition. Katia's case established an important precedent.
- Kaiser, S. and Sachser N. (2005). The Effects of Prenatal Stress on Behaviour: Mechanisms and Functions. *Neuroscience and Biobehavioral Reviews* **29**, 283-294.
- Kruijver, F.P.M., Zhou, J-N., Pool, C.W., Hofman, M.A., Gooren, L.J.G., Swaab, D.F. (2000). Male to Female Transsexuals Have Female Neuron Numbers in a Limbic Nucleus, *Journal of Clinical Endocrinology and Metabolism* **85**(5) 2034-2041.
- Kruijver, F.P.M. (2004). Sex in the Brain – Gender Differences in the Human Hypothalamus and Adjacent Areas; Relationship to Transsexualism, Sexual Orientation, Sex Hormones and Endocrine Status. PhD Thesis. Netherlands Institute of Brain Research, P212.
- Landén, M. (1999). Transsexualism, Epidemiology, Phenomenology, Aetiology, Regret after Surgery, and Public Attitudes. PhD dissertation. Göteborg University.
- Mayer, A., Swaab, D.F., Pilgrim, C., Reisert, I. and Lahr, G. (1998). Genes Involved in Male Sex Determination Are Expressed in Adult Human Brain. *Neurogenetics* **1**, 281-288.
- McLachlan, J. (2001). Environmental Signaling: What Embryos and Evolution Teach Us About Endocrine Disrupting Chemicals. *Endocrine Reviews* **22**(3) 319-341.
- Money, J (1994) The Concept of Gender Identity Disorder in Childhood and Adolescence After 39 Years. *Journal of Sex and Marital Therapy*, **20**(3), 163-177.
- Ochoa, B. (1998). Trauma of the External Genitalia in Children: Amputation of the Penis and Emasculation, *Journal of Neurology* **160**(3-11) 1116-1119.
- Parks, J.S. (1977) Cognitive Style and Gender Role in Persons with Sex Chromosome Aberrations, *Hospital. Practice* **12**(10), 93-102, 107-108.
- Rangecroft, L., Brain, C., Creighton, S., Di Ceglie, D., Ogilvy-Stuart, A., Malone, P., Turnock, R. (2001). Statement of the British Association of Paediatric Surgeons Working Party on the Surgical Management of Children Born With Ambiguous Genitalia.
- Rosenhan, DL. (1973) On Being Sane in Insane Places, *Science* **179**(70), 250-258.
- Sobel, V., Imerato-McGinley, J. (2004). Gender Identity in XY Intersexuality. In Child and Adolescent Psychiatric Clinics of North America (Sex and Gender). Milton Diamond and Alayne Yates (editors); W.B. Saunders, Philadelphia. **13**, 609-622.
- Swaab, DF. (2004) Sexual Differentiation of the Human Brain: Relevance for Gender Identity, Transsexualism and Sexual Orientation
- Walter, S., Hurwitz, I., (1970). Psychosexual Ambiguity in Klinefelter's Syndrome *Semin Psychiatry*, **2**(1), 53-64.
- Wilson, G and Rahmen Q. (2005) Born Gay – The Psychobiology of Sex Orientation, Peter Owen Publishers, London.
- Zhou, J-N., Hofman, M.A., Gooren, L.J.G., Swaab, D.F. (1995); A Sex Difference in the Human Brain and its Relation to Transsexualism. *Nature* **378**, 68-70.