localities, particularly during the transmission months following rains. Breeding opportunities for *Aedes aegypti* are enormous and evenly spread in most Delhi in the form of desert coolers, water storage tanks, leaking water supply, fountains, wells, tire dumps, and rain water collection on roof tops and a variety of receptacles. Vector control under the urban malaria scheme is erratic and limited to some localities by way of spraying of larvicides in surface drains, temephos treatment of water tanks and thermal malathion fogging. Field operations are wanting and mainly targeted to control *Culex* breeding. Malaria is endemic in Delhi and the vector *Anopheles stephensi* and *Aedes aegypti* largely share similar breeding habitats. DHF epidemic coincides with *P. falciparum* prevalence making diagnostics a problem. Dip-stick test[2] for *P. falciparum* would be desirable. While malaria is treatable, there is no specific treatment for viral infections. In dealing with DHF preventive vector control is the key to success. This is attainable by a well-organized *Aedes* control programme. The control of *Aedes aegypti* by chemical methods like spraying and fogging or ULV application is not productive and sustainable[3], except epidemic control[4]. *Aedes* control requires strong entomological support which is weak in the states and almost non-existent in the municipal corporations and smaller bodies[5]. The disease has come to stay and governments would do well by emphasizing community participation and taking help of legislative measures. The approach to DHF control should be community based directed towards species sanitation and learning from the DHF endemic countries.

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Sex and the single X

In mammals, including human, it is believed that the Y chromosome by its presence or absence exerts a series of actions upon which develop the sexually dimorphic characters. Although a number of genes in this cascade of binary decision might be autosomal or X-chromosomal, there must be one or more gene(s) on the Y chromosome to govern the process of testis determination if the male development is a dominant pathway.

SRY is the only gene that is required on the Y chromosome for testis determination as the introduction of transgenic *SRY* alone into chromosomally female mice results in male development[1]. Recently a few autosomal genes have been identified that are probably involved in testis development. For example, mutation in *SOX9* gene is associated with XY sex reversal in human[2] and the null mutant for the gene *SF-1* shows severe abnormalities in the gonadal development of mice[3]. In contrast to our current understanding of the process of male development in mammals, the genetic cascade of the female pathway is almost completely unknown. It is possible that in some of the XY females, a 'loss-of-function' mutation in a gene that inhibits ovarian development (in males) could have been the cause for sex reversal. Although chromosomal deletion in 9p and 10q is associated with such XY females, interruption of testis development was viewed as the cause for sex reversal having led to the female development by default[4]. However, that the ovarian differentiation may not be a passive one is indicated by the fact that in wood lemmings, rearrangement in an X chromosome induces the development of reproductively active XY females even in the presence of a normal Y chromosome[5]. More interestingly, in two species of mole-vole, sex determination is in the absence of Y chromosome (XO male; XX female)[5,6]. The first indication for involvement of an X chromosomal gene in human sex determination was provided by the identification of a family with an X-linked mode of inheritance of 46,XY sex reversal[7]. Demonstration of duplication in short arm of the X chromosome (Xp21 region, called the *DSS* locus) in such 46,XY females raised the interesting possibility that the duplicated X chromosomes cause XY sex reversal by expressing double dose of a gene normally subject to X inactivation[8]. However *DSS*-negative 46,XY males develop testis and show normal external genitalia, indicating *DSS* is not involved in testicular development[8]. Therefore, it is puzzling to imagine how the inactivation of X chromosome and the dosage activity of this locus control gonadal development.

Recently Jimenez *et al.*[9] discussed an appealing model for the dosage effect of *DSS* speculating a female determining function for the *DSS*. It is proposed that in normal female the *DSS* down regulates autosomal genes involved in male development (e.g. *MIS*) but the autosomal factors are not inhibited in the 46,XY males owing to the suppressive action of *SRY* on *DSS*. Thus, testis development implies inhibition of female pathway genes and for the ovarian development, the male pathway genes must be suppressed. Therefore, deletion of *DSS* does not affect male development. However the duplication of *DSS* in XY individuals [46,XY *dup*(Xp)] renders the level of SRY protein insufficient to suppress the two active doses of *DSS*, thus leading to development of female phenotype. It is likely that such a dosage effect might have been the primitive mechanism of sex determination in mammals and that *SRY*'s role is a recent addition because some of the events of sexual differentiation in the primitive mammals, marsupials, are based on the ratio between X chromosome and autosomes[10]. In fact the effect of dosage

in sex determination has earlier been shown for birds (the group that diverged from the same ancestral stock of mammals) although here it is based on the Z chromosome to autosome ratio[11]. Therefore, Chandra, by extending his original hypothesis on dosage effect in mammalian sex determination, viewed the absence of dosage compensation for Z chromosome as a key factor in the avian sex determination[12].

While the *DSS* dosage model[9] is attractive because it resolves the paradox of 46,XY *dup*(Xp) sex reversal and offers an evolutionary perspective as stated above, but the support for this model at present is very little. Moreover there are a few points to be considered before suggesting such a sweeping role for *DSS*. First, there is no evidence for *SRY* to be an inhibitor of *DSS*. Should that be so in all the mammals then, in the mole-vole *Ellobius*, which lacks Y chromosome and *SRY* (ref. 6), there should be no males. Likewise, in human while *DSS*-negative males are normal, the effect of such a genotype on genetic female is not clear due to the random X-inactivation. Moreover the proposed negative regulatory role of *MIS* (a male pathway gene) on 'female pathway genes' and of ovarian germ cells on 'male pathway genes' in sex differentiation is questionable since in the *MIS*-deficient mice, testis is spermatogenically active[13], and the gonadectomized females are phenotypically normal with little obvious effect of the absence of germ cells[14]. A role for *DAX-1* (the gene which falls in the *DSS* region and code for a nuclear receptor) in gonadal determination is not clearly established since no rearrangements in *DAX-1* could be detected in thirty 46,XY females[7]. Nevertheless, the occurrence of *DSS*-deleted males and duplication of *DSS* in 46,XY females emphasize that *DSS* is necessary for ovarian development and may be repressed in XY individuals.

The recent progress in the identification and characterization of genes like *SF-1*, *SOX9* and *WT1* (ref. 16), which show multiple functions in addition to their role in gonadal differentiation, reveal a multi-factorial hierarchy in the cascade of gonadal determination. Moreover, testis development in XX–XY chimeras with atleast 25% XY cells[17], high incidence of XX sex reversal for *SRY*-transgenes in homozygous condition rather than in hemizygous, correlation of incomplete penetrance of *SRY*-transgene with a lower level of its transcripts[16], and duplication of *DSS* and XY sex reversal[8], all suggest a concentration threshold for sex-determining factors in the gonadal development. Therefore, it is reasonable to explain that, instead of assuming the 'one-gene one-function' role of *SRY* in suppressing only the *DSS*, there may be opposite and competitive (indirect?) effects of *SRY* and *DSS* likely on one or more critical factor(s) whose concentration may determine the gonadal switch. Doubtless the switch must function in association with other factors as well as their developmental timing. Further experiments including the construction of animals carrying additional copies of *DAX-1* will be required to understand the process of ovarian determination and the role of *DSS* in it. It may also lead to the discovering of putative additional factors. Moreover the 'default' pathway of ovarian development in mammals should be reconsidered to identify critical genes for ovarian determination, if any.

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