



Figure 2. The effects of progressive loss of X-linked alleles on a hypothetical signaling pathway. The diagram shows successive components of the pathway as colored discs, each put in place by the actions of enzymes a, b, c, and d. The size of the discs is proportional to the amount of each component (level 1). The model proposes that enzymes a, b, and c are all encoded by genes on the X chromosome, and early in evolution were encoded by genes on the two proto-X chromosomes. Alleles are lost as the proto-X progressively degenerates, eventually forming the gene-poor Y chromosome (Fig. 1). A twofold reduction in the amount of an enzyme is likely to cause a reduction in its product, although not necessarily twofold. The cell's normal homeostatic mechanisms are likely to correct small disturbances and there is likely to be little or no effect on subsequent steps in the pathway (level 2). Even the loss of two enzymes may be corrected with no physiological effect (level 3). However, a stage will eventually be reached when the cumulative effects of enzyme (gene) depletion cause key components to decrease below a critical level and trigger an effect on phenotype (shown here on level 4). Selection pressure will be exerted to correct the phenotypic effect, most readily by up-regulating expression of one or more of the remaining, single alleles of enzymes a, b, or c.