diurnal rhythm in early puberty with an increase that starts in the night after the first pulse of luteinising hormone, peaks at approximately 0600,[7] and falls to below 2 nmol/L by midday. In boys in early puberty, this variation explains why early morning erections are common and why serum testosterone measurements taken during afternoon clinics are a useless investigation.

Recent knowledge from the study of inborn errors of metabolism has shown that oestrogen is the predominant hormone that causes epiphyseal closure in both sexes. Men with mutations of the genes for oestrogen-receptor α[8] or P-450 aromatase[9,10] continue to grow after the age of 20 and attain tall stature. Non-specific aromatase inhibitors, such as testolactone, have been used in paediatric endocrine practice for many years to block the conversion of testosterone to oestrogen. Wickman and colleagues have refined this intervention by the use of a specific aromatase inhibitor to mimic the effect of these inborn errors. When testosterone therapy is combined with an aromatase inhibitor, the former provides virilisation and a growth spurt, while the latter delays epiphyseal closure thus allowing growth over a longer time. Indeed, the effect of this double-edged therapeutic approach is magnified because combined therapy produces a higher serum testosterone and lower serum oestrogen concentration than would be attained by either agent alone. The overall effect is to advance pubertal development and improve the final-height potential.

Theoretically, the use of an aromatase inhibitor should decrease the incidence of unwanted gynaecomastia, which is a common accompaniment to testosterone treatment due to conversion of testosterone to oestrogen. Wickman and colleagues' study was too small to assess the effects on gynaecomastia, although serum oestradiol concentrations were significantly lower in the letrozole group. Small numbers, and the short duration of the study also limited the possibility of finding significant differences between groups in changes in segmental proportion and spinal growth. Although small, the study has power from its design (randomised, double-blind, placebo-controlled). Moreover, this study illustrates the successful use of a specific enzyme inhibitor that complements the knowledge of the pathophysiology of growth. Not only is there a potential new treatment for boys with constitutional delay of puberty and growth, but the knowledge may be applicable to other disorders that need to arrest epiphyseal maturation to prolong growth.

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Suppression of unwanted memories: repression revisited?

Memory can be an accurate chronicler of past events, but is also vulnerable to loss and distortion.[1] Forgetting usually occurs imperceptibly with the passing of time. Can people voluntarily forget information by wilfully suppressing it? Recent studies by Michael Anderson and Collin Green[2] say "yes". These experiments have stimulated debate because the researchers suggest that their results may provide "a viable model" for Freud's much maligned theory of repression.[3,4] Furthermore, the results have been linked[5] to the disputed idea that people can repress and later recover memories of childhood sexual abuse.[4,6]

Anderson and Green used a carefully crafted experimental design to isolate the effects of voluntary suppression on tests of memory. Participants learned a list of 40 unrelated word pairs, such as "ordeal-roach" or "moss-north". They were then prompted with the first word of 30 of the pairs. For half of the items, participants were asked to respond with the second word of the pair; for the other half, they were instructed to suppress the word from conscious awareness. Then a final memory test was carried out. The researchers asked the participants to do their best to recall the second word of each pair when presented with the first word, regardless of the earlier instructions to suppress memory for some words. Participants recalled more words from the "respond" group than words from the "suppress" group. This finding alone might simply indicate that the recall of words from the "respond" group had improved because of practice, rather than revealing an impairment of recall for words in the "suppress" group. However, ten of the word pairs that had appeared only on the study list were used as control words. Fewer suppressed words than control words were recalled. This finding cannot be attributed to the practice of recalled words, and indicates that the recall of words from the "suppress" group was indeed impaired. The same outcome occurred even when Anderson and Green paid participants to produce the correct answer on the final test.

These and other experimental manipulations used by Anderson and Green support their finding that voluntary suppression can impair subsequent memory. Do the results also support Freudian notions of repression? And do they imply anything about repression of such traumatic events as childhood sexual abuse?

It is important to recognise that Freud's ideas about repression changed over time.[7,8] Freud's first concept of repression was as an intentional attempt to prevent distressing experiences from entering conscious awareness. Later, he used the term to refer to one of several defence mechanisms that operate automatically outside of a person's awareness. Anderson and Green's data support Freud's early ideas about repression in that

they confirm that intentional suppression can impair memory. However, Anderson and Green's results do not address Freud's later ideas about the involuntary operation of repression. More importantly, Freud's ideas about both voluntary and involuntary repression focused on emotionally distressing experiences. Because Anderson and Green used neutral word lists, their data do not bear directly on this key feature of Freudian repression. Indeed, the researchers explicitly conceptualise voluntary suppression as a general executive control process that is not specifically linked to emotional experiences.

These points are important to remember when discussing the accuracy of repressed, and later recovered, memories of childhood sexual abuse.[4,6,8] Conway[5] suggested that, when people are strongly motivated to try to forget, voluntary suppression would be more likely to inhibit memory for emotional traumas than for innocuous laboratory stimuli. Although people may try to suppress emotional experiences, a motivation to forget may not mean an ability to do so. Pertinent evidence comes from investigations of intentional forgetting among individuals who were sexually abused as children.[9] Some of these individuals had post-traumatic stress disorder and when instructed to try to forget trauma-related words, such as incest, were less able to suppress these words than were individuals without stress disorder. This finding also requires caution in interpretation since the study involved memory for word lists. However, women who reported repressed or recovered memories of childhood sexual abuse showed no special ability to suppress memory of abuse-related words.[10] Overall, these findings are consistent with evidence showing that traumatic experiences typically produce persistent, intrusive recollections that are difficult to suppress.[1,8] Although there are cases in which recovered memories of childhood sexual abuse seem to be accurate,[6,8] the mechanisms of forgetting and recovery remain poorly understood.

Much work needs to be done to clarify whether the type of voluntary suppression documented by Anderson and Green can inhibit memory for emotional experiences. It will also be important to determine whether suppression can operate involuntarily, as envisaged by Freud in some of his writings concerning repression. Anderson and Green's study is a valuable step towards illuminating the mechanisms involved in the suppression of non-emotional experiences.

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Chemokine receptor polymorphism in transplantation immunology: no longer just important in AIDS

AIDS-related research has linked the importance of the biology of chemokine ligands and receptors to HIV-1 susceptibility. An important discovery is that a natural mutation of a receptor for chemokines belonging to the CC family, CCR5, confers on individuals who are homozygous for the expression of the mutant allele CCR5Δ32 high resistance to HIV-1 infection.[1,2] This discovery was based on findings that RANTES (also known as CCL5) and two other CC chemokine ligands, macrophage inflammatory protein-1α and β (MIP-1α and MIP-1β, also known as CCL3 and CCL4, respectively) are the major HIV-suppressive factors produced by CD8 T cells; that CCR5 is the receptor for these ligands; and that CCR5 is the main receptor for M-tropic strains of HIV-1.

CCR5Δ32 is a 32-base-pair deletion within the coding region of CCR5, which results in a frame shift and generates a non-functional receptor.[2] Heterozygosity and homozygosity for this polymorphism occurs in 10–15% and 1% of the Caucasian population, respectively.[2,3] The prevalence of CCR5Δ32, the failure of this allele to be expressed on the cell surface; and the inability of RANTES, MIP-1α, and MIP-1β to bind to this receptor has led investigators to hypothesise that the molecular genetics of this chemokine receptor may affect how the biology of CCR5 and CC chemokines influences other inflammatory or immunologically mediated diseases. Subsequent studies showed that homozygous expression of CCR5Δ32 is associated with reduced risk of asthma and with decreased severity of rheumatoid arthritis and multiple sclerosis.[4-6] These findings support the notion that homozygosity for CCR5Δ32 is associated

Chemokine receptors and their respective ligands implicated in promoting allograft rejection

Chemokine receptors	Chemokine ligands	Organ allograft rejection
CCR1	RANTES (CCL5[1])	Heart[11,13]
	MIP-1α (CCL3[1])	
	MCP-3 (CCL7[1])	
	HCC-1 (CCL14[1])	
	HCC-2 (CCL15[1])	
	HCC-4 (CCL16[1])	
	MPIF-1 (CCL23[1])	
CCR5	RANTES (CCL5[1])	Fischered et al
	MIP-1α (CCL3[1])	
	MIP-1β (CCL4[1])	
CXCR3	MIG (CXCL9[1])	Heart[12]
	IP-10 (CXCL10[1])	
	I-TAC (CXCL11[1])	

RANTES=regulated on activation normal T cell expressed and secreted; MIP=macrophage inflammatory protein; MCP=monocyte chemoattractant protein; HCC=haemofiltrate CC chemokine; MPIF=myeloid progenitor inhibitory factor; MIG=monokine induced by γ-interferon; IP=interferon-γ-inducible protein; and I-TAC=interferon-γ-inducible T cell α chemoattractant.