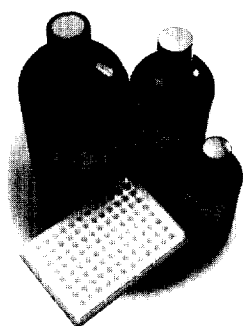


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## Genes and painkillers

Ever taken a painkiller and found that your stubborn headache still persisted? As with countless other biological effects, it could be down to your genes.

According to research reported at the Autumn meeting of the American Chemical Society, held in Las Vegas, the analgesic drug codeine (*O*-methylmorphine) is totally ineffective in some ethnic groups – including one in ten whites. The researchers have uncovered a variety of differences in the drug's efficacy and side effects, based on the user's ethnicity, which could have important implications for prescribing painkillers and in the design of new drugs.

The response and effects of numerous drugs vary from person to person, and in particular the elderly can be more sensitive than others. Clinical pharmacologist Professor Alastair Wood of Vanderbilt University (Nashville, TN, USA) has found that the opiate codeine is unusual because its effects derive not

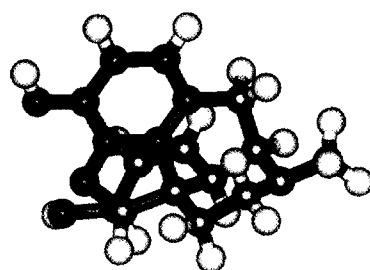
from the drug itself but from the metabolite of the liver enzyme CYP2D6, which converts it to morphine. Wood's research indicates that about 10% of whites lack this enzyme through a genetic deviation, so cannot produce the active material to relieve their pain. When a drug fails to have an effect, physicians tend to simply prescribe more of that drug, but for those people lacking the gene for CYP2D6 this does not work and can be dangerous.

Wood also found that about 2% of Chinese lack CYP2D6. Additionally, even for those who do have the enzyme, its efficiency is much reduced compared with other ethnic groups, so an affected Chinese produces a lot less morphine from a dose of codeine. Furthermore, any morphine produced has, through an as yet unknown mechanism, less effect for the same blood concentration on Chinese than white individuals. Wood also found that in spite of this, Chinese subjects still suffered the potentially nauseating side-effects of codeine.

The liver enzyme CYP2D6 metabolizes a wide range of other drugs including the antihypertensive propranolol, propafenone (for heart arrhythmias), haloperidol (for certain mental illnesses) and several of the commonly prescribed tricyclic antidepressants. These various drugs affect the body directly, so people who are lacking CYP2D6 experience exaggerated effects when taking them rather than the reduced effects seen with metabolite-dependent codeine.

David Bradley

<http://homepages.enterprise.net/bradley/elem1.html/>



*Morphine – a great painkiller.  
But not everyone is getting full  
benefit.*

The 10th Annual **Bristol-Myers Squibb** Award for Distinguished Achievement in Neuroscience Research has been awarded to Drs Eric Shooter (Stanford University School of Medicine, CA, USA) and Hans Thoenen (Max-Planck Institute, Martinsreid/Munich, Germany). The scientists share a \$50,000 award in recognition of their contribution to nerve growth factor research.