

## Cocaine

*Leading causes of death amongst Cocaine abusers include intoxication, homicide, suicide and falls*

Cocaine, derived from the shrub *Erythroxylon coca*, was both chemically extracted and reported to be psychotogenic<sup>1</sup> in 1859. Included in the original formulation of 'Coca-Cola', it was declared illegal under the Harrison Act of 1914.<sup>2</sup> It has been used as a local anaesthetic and in analgesic cocktails. In one study,<sup>3</sup> the main routes of administration were: smoking, 40%; intranasal, 32%; and injecting, 24%; injecting being associated with the highest level of dependence. 'Crack', dating from 1983,<sup>4</sup> is a pure form of cocaine which consists of white crystals that 'crack' into small rocks.<sup>5</sup> Crack is smoked, giving an immediate effect,<sup>6</sup> a rapid rise in blood pressure and a powerful 'hit'.<sup>7</sup> Cocaine blocks dopamine (DA) uptake into presynaptic dopaminergic terminals, causing a great increase in extracellular levels of DA in the nucleus accumbens and activation of the 'reward system'.<sup>8,9</sup> The 'high' in chronic cocaine use is directly related to the amount of striatal DA blockade, and hence the availability of free DA, whereas craving in detoxified cases related to enhanced thalamic response to DA. Withdrawal is due to DA depletion.<sup>10</sup> The enzyme necessary for acetyl choline production is unaffected.<sup>11</sup>

Cocaine abuse may be at least partially genetically based.<sup>12</sup> Underlying personality disorder is likely.<sup>13</sup> Major mental illness is an important vulnerability factor,<sup>14</sup> partly because sufferers live in areas of high usage,<sup>15</sup> and because of self-treatment of symptoms.<sup>16</sup>

### *Clinical aspects*

Cocaine is associated with strong psychological dependence. The effects are a heightened sense of well-being, exuberant mood, a feeling of physical strength, social disinhibition, persecutory ideas or delusions, and an hallucination of motile subcutaneous insect ('formication' or 'cocaine bugs', also found in amphetamine users). Nasal septal ulceration in 'snorters' of cocaine causes whistling speech. Gastric ulcers, weight loss, insomnia, and impaired mental ability are other associations, as are panic attacks.<sup>17</sup> Chronic male co-users of cannabis may experience feminization.<sup>18</sup> 'Snow lights' are sparkling lights seen in the peripheral visual fields.

Physical dependence is possible. Withdrawal is generally mild. With prolonged, heavy use dysphoria commences shortly after drug cessation or reduction: fatigue, unpleasant dreams, insomnia or hyper-somnia, increased appetite, psychomotor retardation/agitation and suicidal feelings. Symptoms peak in two to four days, and may last as little as 18 hours.

Gawin and Kleber<sup>19</sup> divided cocaine cessation into three phases: the 'crash' with craving for sleep; withdrawal, when sleep is relatively normal but the patient craves cocaine - a time of high risk for relapse; and extinction. According to Marzuk *et al*,<sup>20</sup> cocaine is one of the leading causes of death among young adults in New York City because of intoxication, homicide, suicide, and falls. Transient paranoid states occur in some users unrelated to route or dose,<sup>21</sup> and those affected may be more vulnerable to developing functional psychosis.<sup>22</sup> According to Tueth<sup>1</sup>, many abusers are paranoid and are dangerous if armed; continued use may worsen persecutory ruminations; psychosis is less likely with intranasal than intravenous administration; the dose needed to induce psychosis may diminish over time; males are more prone to psychosis; and crack may be a greater culprit than ordinary cocaine.

Cerebrovascular accidents (infarction and haemorrhage) have been reported in cocaine users.<sup>23-25</sup> Myocardial infarction secondary to cocaine use may be due to an adrenergically mediated increase in myocardial oxygen consumption, vasoconstriction, and coronary normal

thrombosis. Chronic use may accelerate atherosclerosis and impair endothelium vasodilator function. In one study of 92 patients who underwent angiography or autopsy,<sup>26</sup> 38% had

coronary arteries. Concomitant cigarette smoking probably compounds the problem. Intravaginal use of cocaine to enhance orgasm may cause ulceration.<sup>27</sup> HIV is common in cocaine users sharing needles.<sup>15</sup>

Cannabis and/or cocaine are common causes of fatal road traffic accidents in American drivers who are alcohol-free.<sup>28</sup> Seizures and hyperthermia also occur.<sup>29</sup>

### *'Body-packing'*

The swallowing of packages of drugs in order to smuggle them, or hiding them in the rectum or vagina, wrapped in something like toy balloons or condoms, is highly dangerous. They may burst, delivering an overdose of drug to the carrier or 'mule', with often fatal results. The diagnosis should be considered if a person has recently been abroad and presents with a bizarre mental state and pyrexia. The drug should be searched for in the urine, and abdominal radiographs are mandatory. The pyrexia is secondary to vasoconstriction, agitation and muscle rigidity, and resetting of the hypothalamic heat regulation centres. Some couriers take benzodiazepines to offset some of these effects.<sup>30</sup>

### *Teratogenicity*

Cocaine use during pregnancy may be associated with prematurity, intrauterine growth retardation, microcephaly, and vasospastic cerebral infarction in the foetus.<sup>31</sup> Postnatal effects include a neonatal neurological syndrome which is usually mild and transient: poor sleep and feeding, irritability, and, convulsions. The new-born has an abnormal electroencephalogram and brain-stem auditory evoked responses which normalise over months. There are worrying reports of sudden infant death syndrome.<sup>31</sup>

### *Neuroradiology*

Positron emission tomography show areas of diminished cerebral blood flow in chronic users,<sup>23</sup> possibly a result of vasospasm.

### *Management*

Prior use of psychotogenic drugs may interfere with the response of psychotic patients to neuroleptics.<sup>32</sup> This is important because of the increasing prevalence of 'dual diagnosis' patients: drug abuse plus functional psychosis.<sup>33</sup> The spending of disability payments on cocaine in the USA by patients with schizophrenia is a major social problem.<sup>34</sup> Such patients may have less negative symptoms but more anxiety and depression.<sup>35</sup> Clozapine may be associated with less substance abuse than are the older neuroleptics in patients with schizophrenia.<sup>33</sup>

Tricyclic antidepressants, such as desipramine, have been used to reduce craving for cocaine.<sup>36</sup> However, these drugs may affect depression more than relapse, and the latter requires a package which includes relapse prevention techniques.<sup>37</sup> Nevertheless, depression scores early during rehabilitation appear related to the high experienced after intravenous cocaine, illustrating the significant potential for relapse in depressed detoxified patients.<sup>38</sup>

Re-exposure to environmental cues previously associated with cocaine use elicits a strong conditioned response with autonomic arousal and increased craving. Such cues cause anxiety with raised levels of ACTH, cortisol, and homovanillic acid, the latter a DA metabolite. Pretreatment with haloperidol, a DA-blocker, reduces these responses.<sup>39</sup> Prevention involves interventions ranging from child-raising to closure of South American cocaine factories.<sup>27</sup>

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