

Abused drug:
OVERDOSE & DEATH

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Dose (劑量, 一服, 一劑)

Dosage (服用的藥量)

Overdose (過度劑量) – too large a dose

- Lethal/Fatal (or deadly) dose may or may not be an overdose!
- An overdose may not be fatal!

WHAT drug?*

WHAT Form?

solid (capsules, tablets, pills)

volatile liquid

solution

aerosol

gas

crystalline suspension

* Lethal factor

WHAT Quantity?*

mg, gm, ml (c.c.)

Any adulterants/impurities?

WHAT Route?*

- Affects Bioavailability – proportion of administered dose of a drug that reaches the circulation
- 1. Injection
 - IV (靜脈)
 - IM (肌肉)
 - SC (皮下)
- 2. Oral
- 3. Sniffed
- 4. Rectal
- 5. Local
- 6. Inhaled

* Lethal factor

Pharmacokinetics (藥物動力學)

- (1) Absorption
- (2) First pass effect

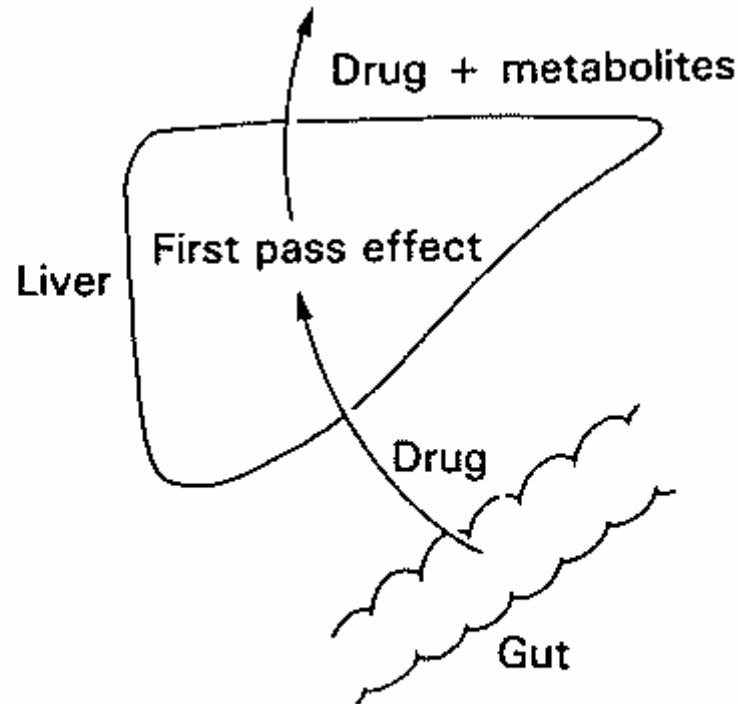


Figure 1.1 First pass metabolism of a drug.

(3) Distribution of the drug

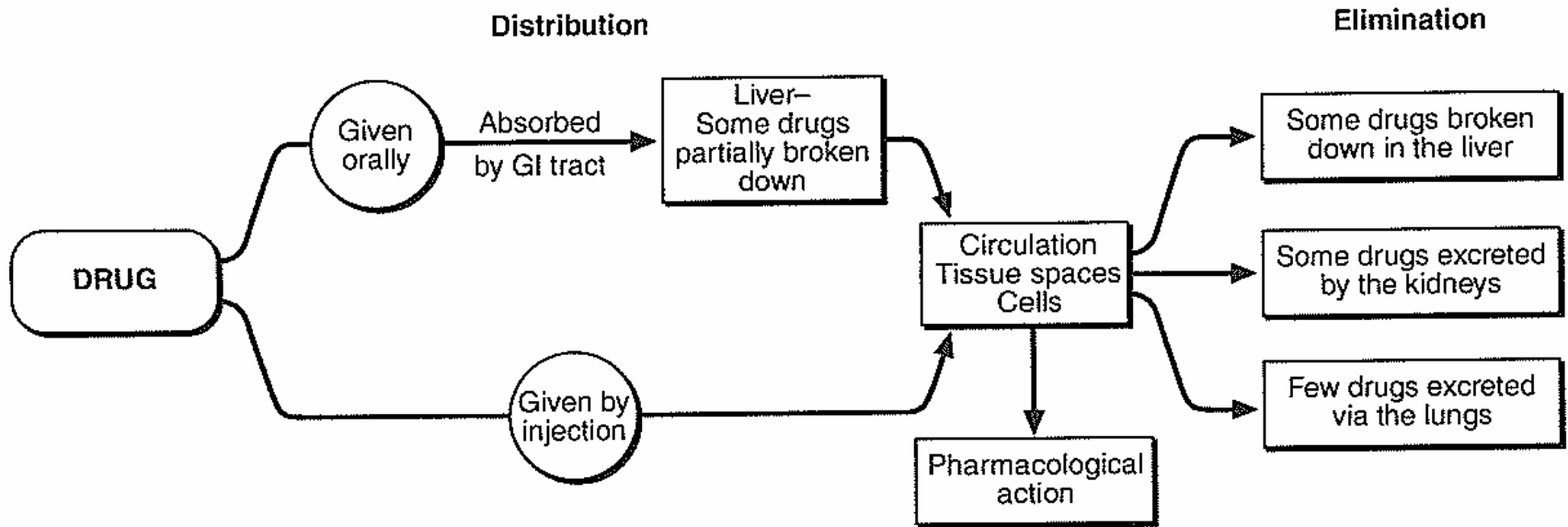


Figure 1.4 Pathways of systemically-acting drugs.

Dose-response curve

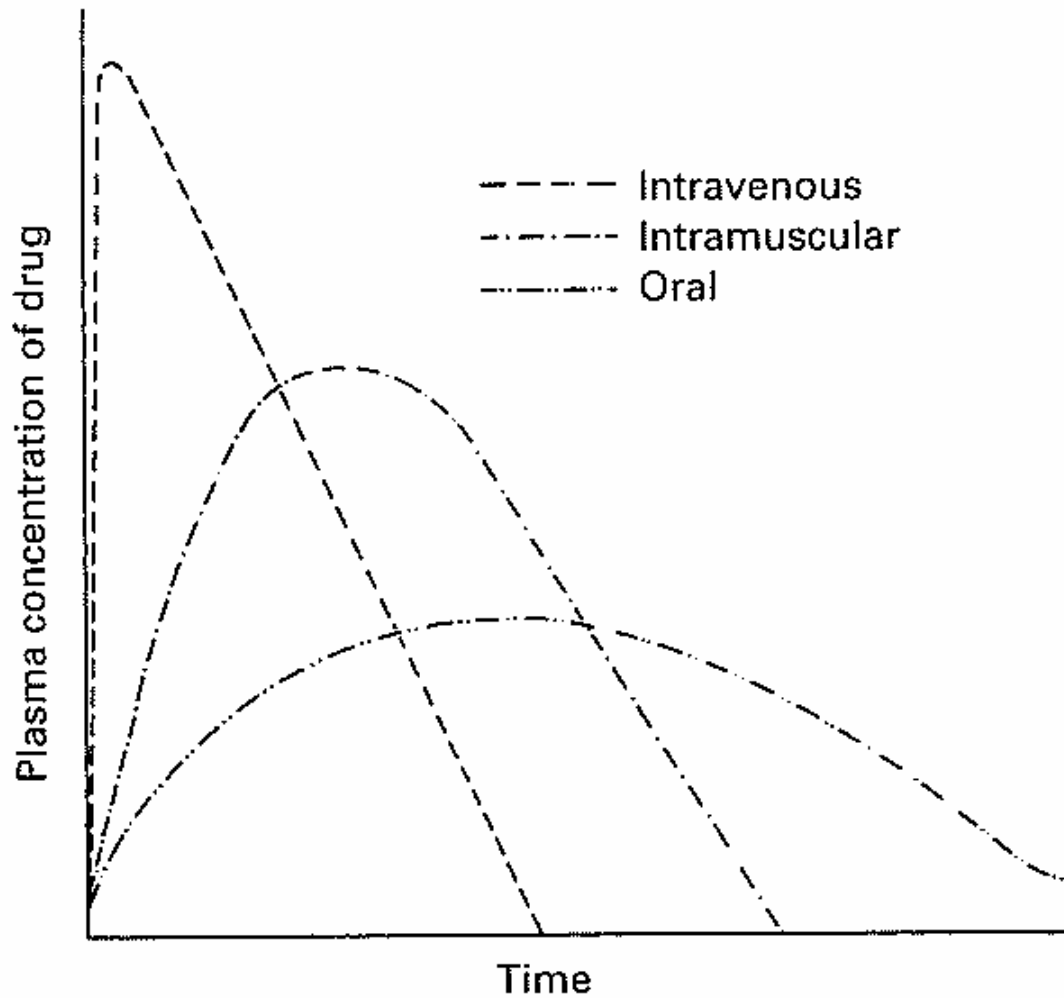


Figure 1.2 The effect of the route of administration of a drug on the plasma concentrations after a single dose.

Distribution of drug influences:

- onset of action
- duration of action

Plasma half-life (半衰期)

Speed of elimination is the main factor to decide the duration of action of a drug & is referred to as the plasma half-life.

“Time taken for a concentration (濃度) after a single dose (usually intravenous) to halve is its plasma/biological half life.”

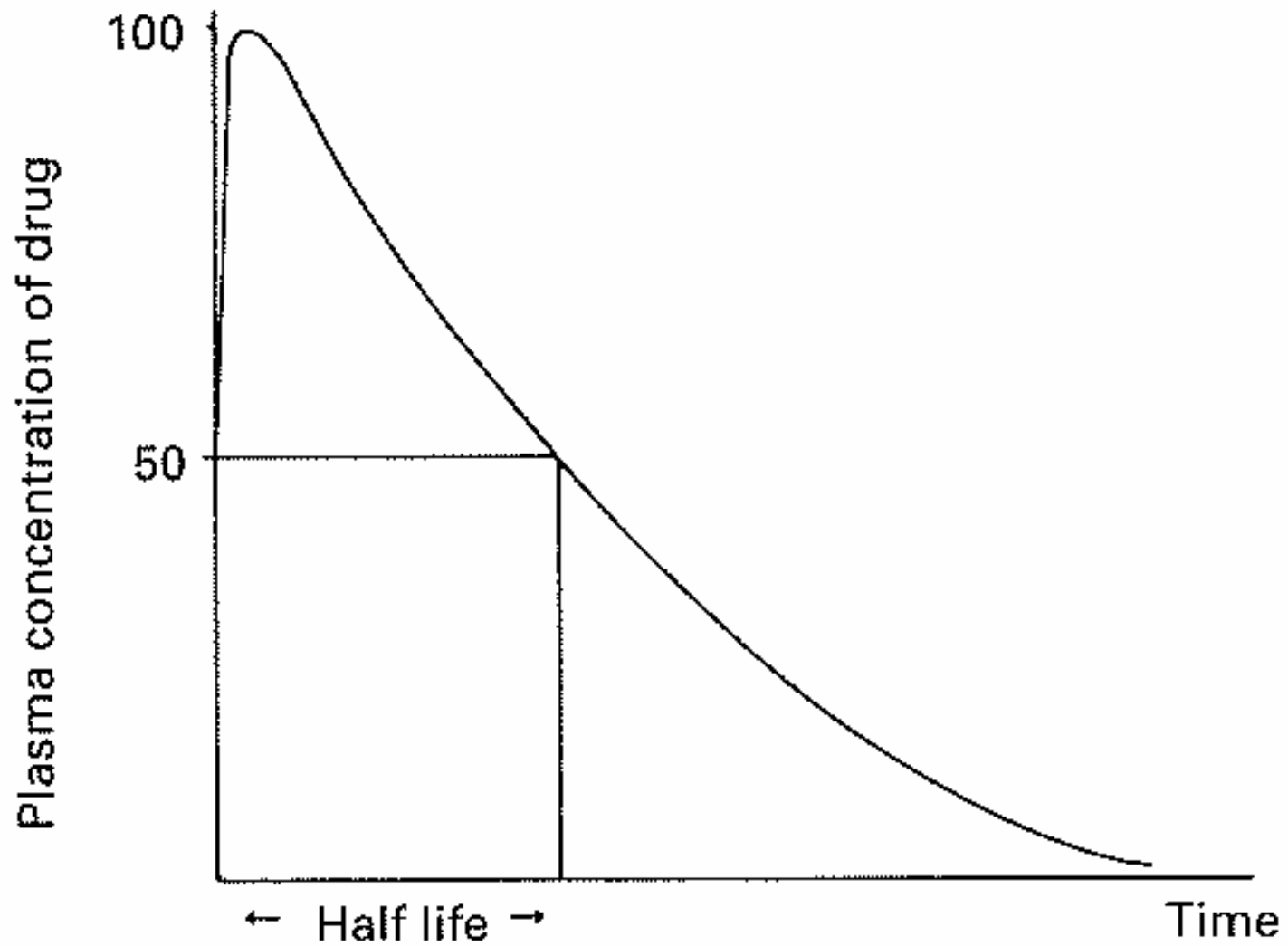


Figure 1.5 Plasma levels and half-life of a drug after a single intravenous injection.

Half life & steady state

Steady state achieved after repeated dosing.

Approximately 5 times the half life of the drug.

Effective dose, lethal dose & therapeutic index

- Lethal doses to 50% of the population (LD₅₀).
- Medium minimum effective dose (ED₅₀).
- Therapeutic index = $\frac{LD_{50}}{ED_{50}}$
(療效指數)

The higher the index, the safer the drug.

(safety ratio 安全系數)

Factors which may modify drug response

Two reasons behind the factors:

1. concentration of the drug in the body, & thus its intensity of action, is subject to individual variation.
2. sensitivity & responsiveness of receptor mechanisms involved in drug action may differ between subjects.

To Continue

The factors

- Size of the subject
- Age of the subject
- Genetic factors
- Nutritional factors
- Race & drug response
- Intercurrent illness
- Drug interactions
- Psychological – Expectation

To Continue

Not Drug A → Response B

but rather

Drug A → Response B

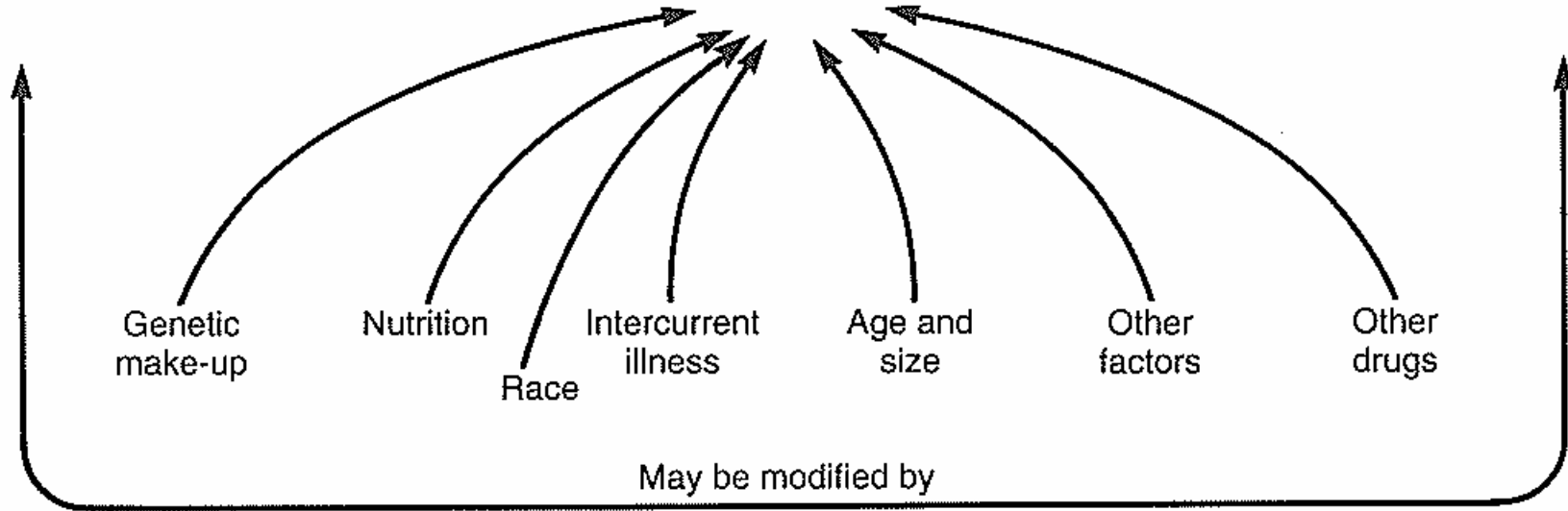


Figure 1.8 Response of a patient to a particular drug.

Lethal & effective doses of abused psychotropic substances

Drug	principle active component	usual lethal concentration in blood (mg/l)	usual lethal dose	usual effective dose	safety ratio
Alcohol*	Ethanol	3600	330g	33g	10
Cocaine	cocaine hydrochloride	5	1200mg	80mg	15
Codeine	codeine phosphate	2.3	800mg	40mg	20
GHB	gamma hydroxybutyrate	300	16g	2g	8
Heroin	Diacetylmorphine	0.3	50mg	8mg	6
Ketamine**	Ketamine hydrochloride	---	2.7g	70mg	38(?)

* Ethanol most common substance in multidrug fatalities
 ** Reported deaths only IV, IM or with co-intoxicant

Drug	principle active component	usual lethal concentration in blood (mg/l)	usual lethal dose	usual effective dose	safety ratio
LSD	d-Lysergic acid diethylamine	4.8ug/L	100mg	100ug	1000
Marijuana	9-tetra-hydro-cannibinol	---	>15g	15mg	>1000
MDMA*	MDMA	3	2g	125mg	16
** Methadone	Di-methadone hydro-chloride	0.7	100mg	5mg	20
** Meth-amphetamine	Meth-amphetamine	2(?)	>150mg	15mg	10
Rohypnol	Fluni-trazepam	0.06	30mg	1mg	30

* MDMA – variability linked to environmental factors

** Methadone – Long half-life a risk factor

*** Methamphetamine – widely divergent reactions to high doses

- **Overdose:**

- toxic overdose
- lethal overdose

How to identify toxic overdose of each abused drug?

- refer to “Protocol of screening and assessment of polydrug abuser” – 2nd edition, Narcotics Division

- **Causes of lethal overdose:**

Some deaths of drug misusers occurred as a result of overdose. Some were suicides but **most were accidents.**

Trend in western countries is upwards.

A caring society is expected to give attention in prevention of premature deaths.

- **Society must be aware that:**
 - A. Drug misuse is a life-threatening condition.
 - B. Drug interactions are important and interaction between alcohol and illicit drugs must be paid attention to.

- A. Immediate deaths related to drug misuse
- B. Responding to overdose (poisoning)
- C. Strategies and preventive measures for reducing overdose harms including death
- D. Local combination of abused drug

A. Immediate deaths related to drug misuse:

- the most important factors which determine whether a misusers would succumb to the toxicity of a drug, is its actual properties and the amount used.

Myth 1: for abused drugs, there is no differentiation between soft and hard.

- another risk factor can be the purity of the drug. The contaminants with which drugs have been diluted or cut, may on occasion have contributed to risk but this factor has been exaggerated.

Myth 2: The contaminants of abused drug is very risky and lead to death.

- Injection of drugs carries high risks of many kinds. Intravenous injection potentially is the most toxic method due to rapid onset of peak levels of drug.

- With oral intake, there is slower absorption and broken down by liver in many cases, therefore generally less toxic, but ingestion of a lethal dose is relatively easy.

- Heroin misuse is still the predominantly important cause of acute drug-related deaths.

Myth 3: Heroin misuse is less common nowadays and those died of it are lesser.

- Loss of tolerance plus use of previous customary dose appears to an important factor in many opioid deaths.

- Methadone has a natural variation in its toxicity as between people.

- Prescription or illicit sale of a “tolerant” dose of methadone to a naïve subject is an important and avoidable lethal factor.

Myth 4: Methadone is a very safe drug to substitute for heroin.

- The most common way in which drugs cause immediate deaths is through their effect on respiration. Reduction of the heart's output can result from a number of different effects of drugs. Certain drugs can result in stroke.

- Of lesser frequency are misuse drug effect on liver, kidney causing death.
- Injection can result in septicaemia and infection of the heart valves, besides transmission of virus infection.
- It must be noted that there is relationship between drug misuse and deaths due to accident or violence, and suicide.
- Injection of some opioid analgesic ground-up tablets of Diconal, DF118, Temgesic (buprenorphine) can block blood vessels.

- No report of acute death directly related to toxicity from cannabis.
- Cocaine can cause sudden death through bleeding from a pre-existing brain aneurysm, great elevation body temperature, agitated delirium with its fatal consequences.
- MDMA, there are a few deaths each year due to disorders of the heart rhythm, overheating, liver damage, or bleeding in the brain.

Myth 5: MDMA is very dangerous drug.

- MDMA and subsequent water intoxication that lead to death can be avoidable.

Myth 6: MDMA with its subsequent dehydration needs a large intake of water.

- Benzodiazepines contribute to drug related deaths through fatal respiratory depression, particularly so when these drugs are taken with opioids or alcohol.

- Amphetamine causes toxicity as a stimulant but it makes a small contribution to drug related deaths.
- LSD does not cause toxic deaths.
- Alcohol can kill young people in a number of ways.

Myth 7: Alcohol only cause death by chronic disease.

- Interaction between several different drugs taken at, or around, the same time. The result is unpredictable. Alcohol often makes a contribution to these interactions.

B. Responding to overdose (poisoning)

1. On receiving the call for assistance:
 - try to establish what has happened as drug involved, ongoing dangers, state of the patient
 - advise the caller to stay with the patient till you arrive
 - if the patient is unconscious, arrange for ambulance to meet you at the scene

2. Assessment of the unconscious patient and the need for basic life support

- airway patent
- breathing satisfactory
- circulation adequate

Resuscitation takes priority over everything else.

3. If breathing is depressed and opiate overdose is likely, give naloxone 0.8 – 2 mg IV every 2-3 minutes to a maximum of 10 mg.

4. General examination

- BP
- pulse
- temp
- pupil response
- injury
- evidence of IV drug abuse
- level of coma

5. If patient is unconscious, turn into the recovery position.

Recovery position

This allows the tongue to fall forwards, keeping the airway clear

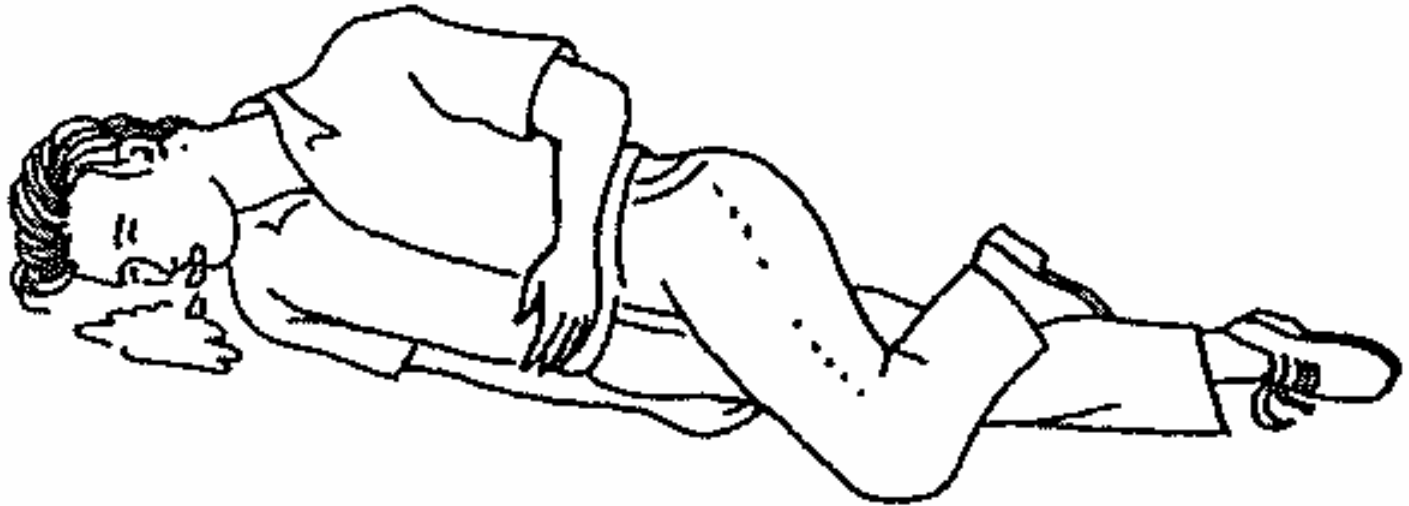


Figure 29.2 Recovery position

6. Collect information:

- drug(s) taken with as much detail as possible
- time of incident
- duration of exposure/amount taken
- route
- intentional or accidental
- general history from attendant

C. Strategies and preventive measures for reducing overdose harms including death

- Identify the drugs which are currently of most concern as causes of immediate drug-related deaths – heroin, methadone, BZD. Volatile solvent can kill young people
- Prisoners on release from goals and clients who have been detoxified or who are completing residential care, are given warning against the danger of loss of tolerance

- Message like “Don’t inject, injecting is too dangerous” becoming drug treatment agency’s culture – repeated, calm and rationally stated. It should be a message to wider population
- Prescribing practice of doctors, if irresponsible, should be reported to Medical Council
- GP should avoid prescribing BZD as far as possible to new patients, and help patients to come off them

- Message that combined use of opioids, BZD and alcohol is dangerous
- Training of drug workers in risk assessment of drug related deaths, resuscitation technique, and naloxone kept on site
- Drug Information should be handed out to all presenting drug abusers, giving relevant health advice.
- Relatives & friends likely to witness an overdose should be given guidance

- Drug agencies should be more active in bringing to the attention of their clients the risk attached to drugged driving
- The aftercare of drug using prisoners should be identified, community liaison established, individualized care plans put in place.
- A high proportion of people who are arrested by police are drug takers. Police force should be given guidance on how to identify and deal with this problem

D. Local combination of abused drug
(Quarterly return of abused drugs in cases reported in July 2006)

Ketamine (K)

K + Cocaine

K + Diazepam

K + Methaqualone

K + Barbitone

K + MDMA

Heroin (H)

H + Methamphetamine + Midazolam

H + Midazolam

MDMA

MDMA + Methamphetamine

MDMA + Ketamine

Methamphetamine (M)

M + Cocaine

M + Ketamine

M + MDMA

M + Diazepam

Benzodiazepine (BZD)

Midazolam + Morphine

Midazolam + Heroin

Midazolam + Diazepam

Diazepam + Quinalbarbitone

Nitrazepam + Nimetazepam

TAKE HOME MESSAGE

1. The range of safety ratios of abused drugs is wide. The ranking of them is accepted element of risk assessment and management.
2. Although the toxicity of a drug may be comparatively low, other lethal and non-lethal factors (e.g. neurological complications, pulmonary diseases, dependence) must be considered.

3. The probability of adverse effects is increased substantially when more than one substance is administered.

example: Alcohol + BZD,
Heroin + non-morphine drugs

4. The risk of overdose is increased when the users repeat administer the drug – user may achieve mistakenly that the initial dose is ineffective or no larger present in the body.

example: MDMA
Methadone

5. Non drug variables can significantly alter toxic reaction. The psychological effects of environment, diet, physical exertion and stress have significant impact on drug reactions.
6. At relatively low non-toxic levels, psychoactive substances may induce dangerous performance decrements. Don't underestimate drugs of large safety ratio.

7. Drug education programs must utilize evidence based prevention messages to counter the human attraction to chemical alteration to consciousness, mood & perception.

8. Monitor fatalities due to abused drug(s) in the local community and think of strategies to control it.

Should “Harm Reduction” be added to the 5 pronged attacks to drug abuse in Hong Kong.

- (1) Preventive Education & publicity
- (2) Legislation & law enforcement
- (3) Treatment & rehabilitation
- (4) International collaboration
- (5) Research

(refer to “The Harm Reduction Manual”,
The Hong Kong Council of Social Service, 2004)

Thank you