AUSTRALASIAN FACULTY OF MUSCULOSKELETAL MEDICINE

SHORT NOTES ON LOCAL ANAESTHETICS

prepared by

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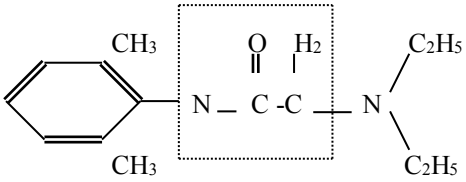
CHEMICAL STRUCTURE

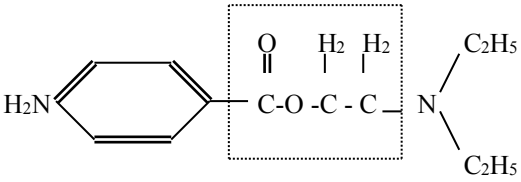
Local anaesthetics are formed by aromatic and amino residues linked by either an amide or an ester.

AROMATIC **AMIDE** AMINO

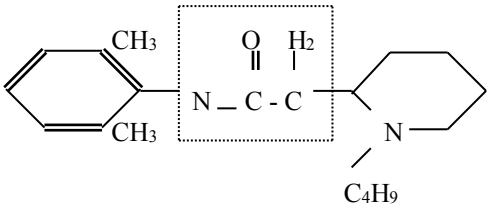


lignocaine

AROMATIC **ESTER** AMINO



procaine

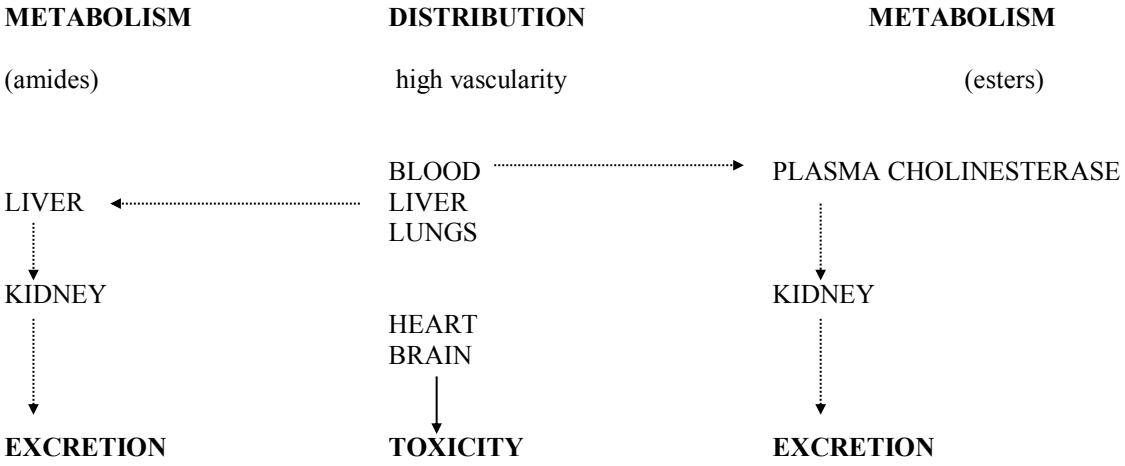


bupivacaine

Why should we know the chemical structure of local anaesthetics?

1. In the first instance, the difference between AMIDES and ESTERS predicates their different metabolism.

All local anaesthetics are distributed similarly to regions of high vascularity, but they are metabolised differently, i.e.



TOXICITY		
CVS	Suppression	Atropine 0.6 mg Ephedrine 12.5 mg - 25 mg Adrenaline
CNS	Excitation	Diazepam 5 mg - 10 mg Thiopentone 50 mg Suxamethonium
ALLERGY		Adrenaline 0.05 mg - 0.1 mg

2. In the second instance, the similarities of local anaesthetics predicate a systematic approach to their pharmacokinetics. Recall the Henderson-Hassellbach equation.

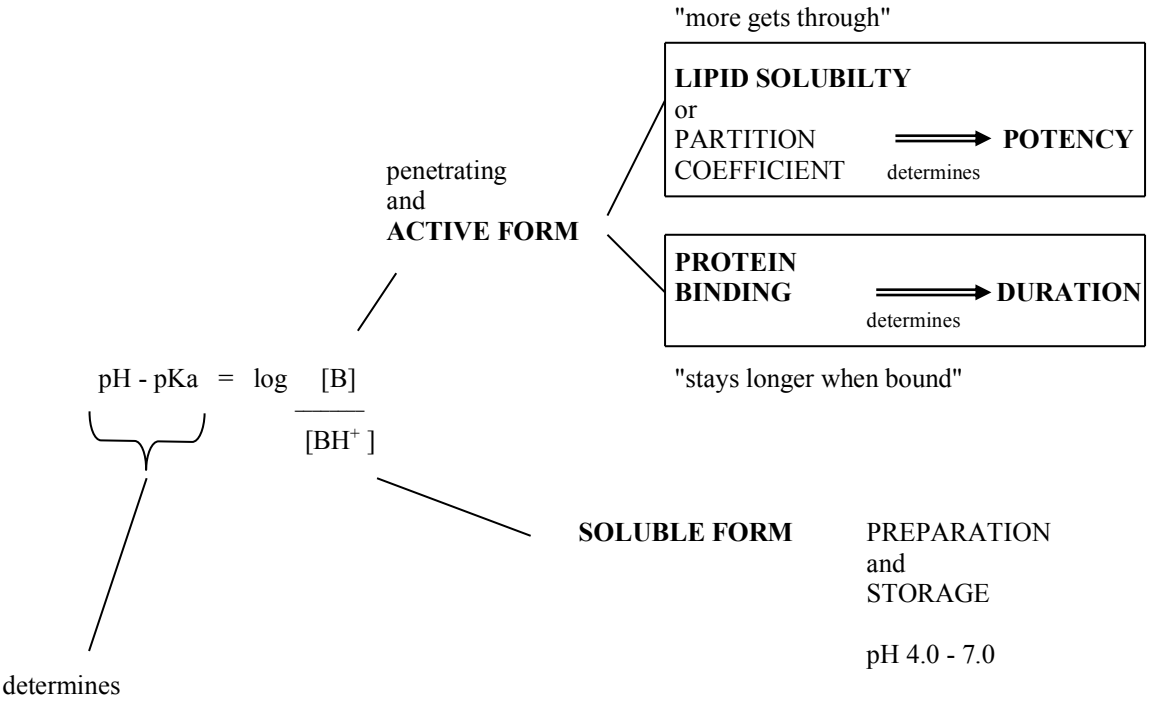
$$B + H^+ \Leftrightarrow BH^+$$

$$\frac{[B]\,[H^+]}{[BH^+]} = Ka$$

$$\log Ka = \log [H^+] + \log \frac{[B]}{[BH^+]}$$

$$\mathbf{pH - pKa = \log \frac{[B]}{[BH^+]}}$$

This latter expression provides the basis for the various pharmacokinetic properties of local anaesthetics.



FRACTION AVAILABLE as [B]

Typical pK ≈ 7.9 ± 0.2

e.g.

if pKa = 8.1

pH - pKa = 7.2 - 8.1
= - 0.9

$10^{-0.9}$ = 1 / 8 i.e. only one eighth of the is available as the active form

if pKa = 8.9

pH - pKa = 7.2 - 8.9
= - 1.2

$10^{-1.2}$ = 1 / 15 i.e. only one fifteenth of the is available as the active form

Note that if the drug is stored at pH 4.0, and the pKa is 7.9

pH - pKa = 4.0 - 7.9
= - 3.9

$10^{-3.9}$ ≈ 1 in 10,000 i.e. virtually all of the drug is in the soluble but inactive form.

The **change in pH** that occurs when the drug is **injected** is what allows it to transform into the **active form**.