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IMMUNOTOXICOTHERAPY : PRESENT STATUS AND FUTURE TRENDS

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ABSTRACT

Immunotoxicotherapy (ITT) is currently used in humans for the treatment of snake venom and cardiac glycoside poisoning. Other toxins have been studied in animals or in vitro to assess their suitability as candidates for detoxification by specific antibodies. Testing conditions are often empirical suggesting that numerous improvements need to be introduced in ITT. Basic mechanisms in ITT include three phases : sequestration, extraction and elimination. The pharmacokinetics of these three phases depend on the type of antidotal binding site (ABS). IgG or its Fab_2, Fab or Fv fragment are the possible choices. The Fab fragment is the most frequently used ABS because of its diffusion properties in the peripheral compartments and its renal excretion by glomerular filtration. Toxicokinetic and pharmacokinetic considerations indicate that the dosage cannot be satisfactorily calculated from stoichiometric principles. Study of the toxin dose-lethality curves shows that ABS dosage can be lowered. Moreover, clinical data reveal that some Fab fragments are directly eliminated without acting on toxin molecules. In order to counteract these drawbacks, a compromise between dosage and duration of infusion is suggested. Other improvements will stem from advances in immunologic methodology. Monoclonal and chimeric antibodies are new tools that will help resolve the clinical problems of immunogenicity and adverse reactions associated with polyclonal ABS.