data which do not go beyond the half response point. If the multiplier which standardizes y is l, then:

$$\sum\left[\frac{-\ln\left(\frac{1}{y_i l}-1\right)}{\ln x_i}\right]-\frac{n}{\Sigma(\ln x_i)}\sum\left[-\ln\left(\frac{1}{y_i l}-1\right)\right]=0$$

can be used to find the best estimate of l. It can be shown that this function is applicable whether 'rate' or 'occupancy' theories of drug action describe the data, using the formulae given by Paton (1961).

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Use of a digital computer programme as a guide to the prescribing of kanamycin in patients with renal insufficiency

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The antibiotic kanamycin may induce serious and permanent adverse effects expecially if high serum concentrations of kanamycin develop and are sustained. The elimination of kanamycin is dependent on renal function and patients with renal insufficiency are particularly prone to cumulative toxicity.

In view of this risk a computer programme written in 1900 Fortran for operation on the ICL 1901A computer has been devised to recommend kanamycin dosage schedules for individual patients with renal insufficiency.

The programme is based upon published studies of kanamycin absorption, distribution and excretion (Welch, Wright, Weinstein & Staffa, 1958; Orme & Cutler, 1969).

Estimates of distribution volume and serum kanamycin clearance are derived from clinical and laboratory measurements which are made routinely on each hospital inpatient with renal insufficiency. Safeguards have been incorporated in an attempt to minimize the effects of accidental loss of a part of a 24 h urine collection.

The input data includes the patients' age, sex, body weight, estimated net protein intake, blood and urine urea concentration, serum and urine creatinine concentration and 24 h urine volume. The input also includes the amounts, times and dates of kanamycin doses already administered to the patient.

The output includes the hypothetical serum concentrations of kanamycin at 2 and 12 h after each dose already given. The computer then proceeds to recommend a series of the largest doses of kanamycin which may be given at 12 h intervals without the 2 h hypothetical serum concentrations exceeding an arbitrary upper limit of 30 μg/ml.

In a prospective study the validity of the programme is being tested by comparing the results of serum kanamycin assay by a diffusion method (Garrod & O'Grady, 1971) with the concentrations predicted by the computer (Table 1) in hospital patients

receiving treatment with kanamycin. It is anticipated that further development will ultimately produce a programme which will predict serum kanamycin concentrations with greater consistency and which will be suitable for routine clinical use.

TABLE 1. *Serum concentrations (μg/ml) of kanamycin in hospital patients receiving treatment (a) as predicted by the computer (b) as determined by microbiological assay*

Patient	Body weight (kg)	Renal clearance ml/min		Serum kanamycin concentration (μg/ml) 2 h after previous dose		12 h after previous dose	
		Urea	Creatinine	(a)	(b)	(a)	(b)
1	63	15·2	34·6	27	26	9	7
2	46	10·5	15·0	42	12	1	2
3	60	7·5	25·4	32	27	14	15
				33	25	16	16
4	53	1·6	2·2	49	35	38	22
5	63	0·7	1·0	38	22	29	15

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Pressure reversal of anaesthesia (T)

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Effect of general anaesthetics on the permeability of single bilayer phospholipid vesicles and the antagonism of high pressure (T)

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Pharmacology of cannabis: catalepsy: hypothermia: inhibition of drug metabolism (T)

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