

EXPECTED AND OBSERVED VALUES FOR THE PRESCRIPTION OF VITAMIN B₁₂ IN ENGLAND AND WALES

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There is a considerable literature about the oddities of the prescribing habits of British doctors, the factors influencing them, and the attitudes of doctors to prescription, but there have been, as far as we know, no attempts to compare quantitatively the expected amount prescribed, on the basis of good clinical practice, with that actually prescribed. There are in general three reasons for this—ignorance of the prevalence of common diseases, the lack of specificity of particular drugs for particular diseases, and the lack of standardization of therapy. Such a study requires a drug which is practically specific for one condition whose prevalence is known, and the one which approximates most closely to this appears to be vitamin B₁₂. We should like to stress that B₁₂ was selected for these purely epidemiological considerations and with no malice aforethought. This paper describes an attempt to measure the expected and observed values for the prescription of B₁₂ in England and Wales for the year 1966.

underestimate the annual incidence, but as a considerable error in incidence would cause only a very small change in expected requirements we have not pursued the matter further. For dosage we have felt forced to use two standards—an 'ideal' and a 'reasonable'. The ideal is based on reputable publications prior to 1966, but as the estimates of necessary dosage were falling at that time it was unreasonable to expect all doctors to adjust their maintenance doses quickly so we have calculated the results for what was previously the accepted dosages. The figures are given in Tables IA, B, C, and D which combine these figures with Scott's prevalence figures, corrected for incidence, to give 'expected' prescribed dosage.

We were, of course, aware that B₁₂ could correctly be prescribed for other megaloblastic anaemia or potential megaloblastic anaemia conditions. We were unfortunately unable to establish their prevalence or incidence with any accuracy so we have delayed discussion of this point to a later section.

METHODS AND RESULTS

'EXPECTED' ESTIMATES FOR PARENTERAL B₁₂

The prevalence of pernicious anaemia was established by Scott (1960). We have assumed that there was no significant change in prevalence between his survey and 1966. We also required an estimate of incidence as the dosage for newly diagnosed cases differs from that for maintenance. For this we have relied on the number of new cases diagnosed in Cardiff hospitals among people who lived in Cardiff in 1960 and 1965. These figures may

TABLE IA
ESTIMATED PREVALENCE AND ANNUAL INCIDENCE OF PERNICIOUS ANAEMIA (P.A.), 1966 (I.C.D. 7th revision Cause 290)

	Prevalence of P.A. per thousand (Scott, 1960)	Estimated Incidence Rate per thousand	Prevalence of P.A. excluding New Cases per thousand
England	1.19	0.048	1.14
Wales	1.53	0.062	1.47
England and Wales	1.21	0.049	1.16

TABLE IB

ESTIMATED ANNUAL REQUIREMENTS OF PARENTERAL B₁₂ FOR PREVALENCE OF PERNICIOUS ANAEMIA

	Registrar General, 1966 Population (thousands)	Prevalence of P.A. excluding New Cases per thousand	Estimated Yearly Dosage per Case of P.A. (μg)	Expected Yearly Requirements (1,000 μg)
England	45,374	1.14	Reasonable 12,000	620,716
			Ideal 4,000	
Wales	2,701	1.47	Reasonable 12,000	47,646
			Ideal 4,000	
England and Wales	48,075	1.16	Reasonable 12,000	669,204
			Ideal 4,000	

TABLE IC
ESTIMATED ANNUAL REQUIREMENTS OF PARENTERAL B₁₂ FOR NEW CASES OF PERNICIOUS ANAEMIA

	Registrar General, 1966 Population (thousands)	Estimated Incidence of P.A. per thousand	Estimated Dosage required per Case* (μg)	Expected Yearly Requirements for New Cases (1,000 μg)
England	45,374	0.048	20,000	43,559
Wales	2,701	0.062	20,000	3,349
England and Wales	48,075	0.049	20,000	47,114

*From Shinton (1966); Hertz, Østergaard Kristensen, and Hoff-Jørgensen (1964)

TABLE ID
ESTIMATED ANNUAL REQUIREMENTS OF PARENTERAL B₁₂ FOR ALL CASES OF PERNICIOUS ANAEMIA

	Required for Known Cases (1,000 μg)		Required for New Cases (1,000 μg)	Total Annual Requirements (1,000 μg)
	Reasonable	Ideal		
England	620,716	206,905	43,559	664,275
				250,464
Wales	47,646	15,882	3,349	50,995
				19,231
England and Wales	669,204	223,068	47,114	716,318
				270,182

ESTIMATES OF 'OBSERVED' PRESCRIPTIONS FOR
PARENTERAL B₁₂

This section was more difficult and much more laborious. We had to attempt to measure the amount prescribed in hospitals, in general practice, and in private practice. For hospital prescription all regional and the Welsh hospital boards were contacted and they kindly gave us the details required. The Department of Health and Social Security kindly supplied the details for general practitioners.

In order to obtain an estimate for the 'private practice' sphere we turned for help to a well-known firm (Glaxo Laboratories Ltd.) who, according to the Department of Health and Social Security figures, supplies over 98% of their requirements. They very kindly gave us details of their total sales in England and Wales for 1966 excluding those for veterinary purposes.

Table IIA gives the comparison between expected and observed estimates for B₁₂ prescriptions had all cases of pernicious anaemia been treated within the

TABLE IIA
OBSERVED AND EXPECTED PRESCRIPTION OF PARENTERAL B₁₂ IF ALL CASES OF PERNICIOUS ANAEMIA
HAD BEEN TREATED WITHIN THE N.H.S. IN 1966

	Expected Requirements (1,000 μg) (1)		Observed Amounts Prescribed in 1966 (1,000 μg)			Ratio Amount Observed/ Amount Expected (4/1)
			(2) General Practice	(3) Hospitals	(4) Both	
England	Reasonable	664,275	1,923,878	153,352	2,077,230	3.1
	Ideal	250,464				8.3
Wales	Reasonable	50,995	220,083	16,404	236,487	4.6
	Ideal	19,231				12.3
England and Wales	Reasonable	716,318	2,143,961	169,756	2,313,717	3.2
	Ideal	270,182				8.6

TABLE IIB
EXPECTED REQUIREMENTS AND ACTUAL SALES OF PARENTERAL B₁₂ IN 1966

	Expected Requirements (1,000 μg) (1)		Actual Sales			Ratio Amount Sold/ Amount Expected (4/1)
			Cytamen and Neo-Cytamen (2)	Add Other Brands (3)	Both (4)	
England and Wales	Reasonable	716,318	3,035,628	39,824	3,075,452	4.3
	Ideal	270,182				11.4

TABLE III

OBSERVED AND EXPECTED CONSUMPTION OF PARENTERAL B₁₂ IN ENGLAND AND WALES AND COUNTY OF ODENSE (DENMARK)

	Pernicious Anaemia Prevalence per Thousand Population	B ₁₂ Ratio Amount Prescribed/ Amount Required
England and Wales	1.21*	3.2
County of Odense (Denmark)	1.26†	3.3†

*Scott (1960)

†Pedersen and Mosbech (1969)

National Health Service. It is clear that there is a considerable excess of observed over expected. Table IIb gives expected requirements and actual sales of parenteral B₁₂ in 1966. The difference between total sales and the amount prescribed within the National Health Service is presumably used in private practice. The table shows that the excess of sales over expected requirements is greater than the corresponding figure in Table IIa.

While we were doing this work in this country Pedersen and Mosbech (1969) published a very similar analysis for Denmark (Table III). The two countries seem to be prescribing equally badly— or equally well.

ESTIMATES OF 'EXPECTED AND OBSERVED' COSTS

The costs for the general practice prescriptions were obtained from the Department, and the hospital costs were completed from the details supplied by the various Boards, using 1966 prices for each strength. For estimating expected costs we assumed that new cases occurred in hospital and that maintenance doses were given at home. We have estimated the drug cost of the private sphere by the difference between the total as supplied by manufacturers and the combined total for hospitals and general practice, and paid for at the same rate as in general practice. It is unfortunately impossible to check this figure but we do not believe the error to be large. All these results are summarized in Table IV. The actual costs would, of course, be very much larger if the cost of nurses, syringes, etc. were

TABLE IV

OBSERVED AND EXPECTED EXPENDITURE ON PARENTERAL B₁₂ PREPARATIONS IN 1966, ENGLAND AND WALES

<i>Expected cost</i>		
<i>Maintenance (general practice)</i>	Reasonable	669,204 (1,000 µg)
	Ideal	223,068
	Cost at 11.5d per 1,000 µg	
	Reasonable	£32,066
	Ideal	£10,689
<i>New cases (hospitals)</i>		47,114 (1,000 µg)
	Cost at 4.8d per 1,000 µg	£942
<i>Total expected cost</i>	Reasonable	£33,008
	Ideal	£11,631
<i>Observed cost</i>		
	National Health Service	£121,600
	Hospitals	4,355
	Private practice	36,500
	Total	£162,455
<i>Ratio observed cost/expected cost</i>		
	Reasonable	4.9
	Ideal	14.0

included. We have been unable to make an accurate estimate of this, but it might well increase the cost of excessive prescription by a considerable factor.

REASONS FOR EXCESSIVE PRESCRIPTION

So far we have avoided the difficult problem of how much the apparent excessive prescription is due to action to prevent or treat other megaloblastic anaemias. Although there is no real evidence that cobalamin therapy has any value in conditions other than vitamin B₁₂ deficiency and partial gastrectomy (Shinton, 1966; Heinrich, 1964; Williams, Baume, and Meynell, 1966), a survey of the prescribing habits of a 2,000 random sample of general practitioners in England and Wales in 1967 showed that 33% of all prescriptions for cyanocobalamin and hydroxocobalamin in 1967 were for conditions other than 'pernicious anaemia and other hypochromic anaemias' (I.C.D. 7th revision cause 290). (We are indebted to Intercontinental Medical Statistics Ltd. for providing us with a computer print-out of their information.)

Results are summarized in Table V. It is stressed that this table is based on numbers of prescriptions but careful analysis of the quantity and strength for

TABLE V
PRESCRIBING HABITS IN GENERAL PRACTICE FOR PARENTERAL B₁₂
(Based on number of prescriptions)

	General Practice Prescribing Habits				
	Pernicious Anaemia 290	Other Anaemias 291 292 293	Multiple Sclerosis 345	Herpes Zoster 880	All Other Conditions
England	66%	10%	5%	3%	16%
Wales	75%	14%	— (< 1%)	5%	6%
England and Wales	67%	10%	5%	3%	15%

individual prescriptions shows the average amount for each condition to be roughly equal except those for multiple sclerosis which were about 30% higher than the others.

The main reason for over-prescribing seems to be giving too much for pernicious anaemia. We cannot say whether this is due to over-prescription or over-diagnosis. The 'other anaemias' are a surprising group. There is no evidence of any effect of B₁₂ in hypochromic anaemia. The number of prescriptions for herpes zoster and multiple sclerosis seems difficult to justify. Taking the most generous view possible we were only able to classify less than 1% of the excess prescriptions as justifiable. Neither partial gastrectomy nor coeliac disease was ever mentioned, but we included all 'gastro-intestinal' diagnoses and those related to hypovitaminosis. It seems therefore probable that our previous estimates of excessive prescription were not unreasonable. Our results are very similar to those of Ellis, Nasser, and Wrighton (1970), who published when this work was nearly completed.

ORAL B₁₂ PREPARATIONS

In addition to parenteral preparations many oral preparations are prescribed in the National Health Service. We have good data in the form of cost from the Department of Health and Social Security for general practitioner prescribing of these oral preparations. We have reasonable evidence that the cost of such preparations in hospitals is negligible. We have no information about the private sphere, where such prescriptions may be common. The results are summarized in Table VI. The ratio of excessive prescribing thus rises to nearly 20 and we must assume that this is a gross underestimate as it neglects the cost of syringes and time spent in injecting parenteral B₁₂ and the use of oral preparations in the private sphere.

DISCUSSION

We are very conscious of the imperfections of some of our data. There are unknown gaps between sales and prescriptions, and between prescriptions and consumption. We are also aware in retrospect that 1966 was not a good year to choose as it was a

period of change in ideas about the correct dosage of B₁₂ for pernicious anaemia. We should also be the last to stress the harmful effects due to overdosage of B₁₂ (Høvdning, 1968). Compared with many other drugs, B₁₂ is relatively inexpensive. We also agree that drugs represent a small percentage of the cost of the National Health Service compared, for instance, with hospital costs. We still, however, believe our exercise to have been worth while as it has shown how a substantial financial saving could be made at no cost to health and at considerable saving of inconvenience to patients, doctors, and nurses. It has also demonstrated how we, as a profession, use a drug which is probably as easy to use scientifically as any other drug. If we do this with B₁₂ how efficiently are we using more difficult and more dangerous drugs such as steroids and antibiotics?

SUMMARY

The attempt is made to relate the total national consumption of B₁₂ to that required by the best available scientific evidence. The ratio between observed and expected consumption varies according to the method of calculation from 3:1 to 20:1.

We should like to express our thanks to all officials of the Welsh and Regional Hospital Boards, to the Department of Health and Social Security, in particular to Dr. Kay Daniels and her assistants, and to Glaxo Laboratories Ltd. for very considerable help.

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TABLE VI
OBSERVED AND EXPECTED EXPENDITURE ON ALL B₁₂ PREPARATIONS IN 1966 WITHIN THE N.H.S.

	Actual N.H.S. Cost 1966			Total Estimated Cost for P.A. Only (4) £	Ratio Actual/Required
	General Practice (1) £	Hospitals (2) £	Both (3) £		
England and Wales	226,014	4,355	230,369	Reasonable 33,008 Ideal 11,631	7.0 19.8

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