grade and consider once more whether there is a place for some other grade of specialist. Perhaps this could be a clinical post without administrative responsibilities. Many women would be interested in such permanent career posts, both part- and full-time, and would be willing to take part in necessary duties at all hours. Such posts, as well as part-time consultant posts, would also be of interest to doctors of both sexes who want to pursue interests outside clinical medicine—for example, research or writing.

Possibly certain specialties are unsuited to part-time work. Nevertheless, many of the less competitive and less dramatic areas of medicine could be well served by doctors who would provide continuity of care over longer periods of time than is provided by doctors in the present training grades. A start could be made in these specialties to integrate the work of part-timers into the total service. Staffing structures vary considerably from hospital to hospital, while the volume of work may not vary in the same way. Furthermore, many full-time posts are not *clinically* so, but involve time for research, teaching, study, administration, and various other duties. Therefore it may not be too difficult to reapportion responsibilities. Arie¹⁴ has shown that in the demanding field of psychogeriatrics an excellent service with high staff morale can be provided by part-time doctors. Perhaps work organisation experts could study this possibility in other specialties.

General practice is proving to be a suitable specialty for part-timers, but there is no co-ordinating system for placing doctors seeking work into the available vacancies. This could be remedied simply by a regional or central agency.

In light of the difficulties that highly skilled doctors, even in so-called shortage specialties, are finding in getting career posts and completing training we would recommend women, so far as possible, to avoid esoteric specialties where few posts exist. This course of action also means that an unexpected change in circumstances need not totally disrupt a career. Until definite arrangements are made for engagement of part-time doctors in the other specialties women who are uncertain about their career wishes should be advised to consider general practice. There are indications that medical care is likely to move towards decreasing

sophistication as financial costs increase, and this may make the outlook for the very highly skilled specialist in a narrow field even more uncertain.

Women will wish to have different work commitments at various stages of life, but complete flexibility is clearly impracticable. Women doctors seem to need part-time posts of between five and eight sessions at all levels of work. Women may be expected to remain in the non-consultant training grades for about twice as long as a full-time worker would stay. Some would then (or after completing training posts full-time) want to work in part-time consultant or other permanent posts for a few years. Many would then apply for standard full or maximum part-time posts. It is now not unusual for consultants to change posts after a few years' service or change between maximum part-time and full-time contracts. By analogy, a change between posts offering different sessional commitments, by women at different stages of career and family development need not cause disruption of services.

References

- ¹ *BMA News Review*, 1975, 1, 55.
- ² Jeffreys, M., and Elliott, P. M., *Women in Medicine*. London, Office of Health Economics, 1966.
- ³ Lawrie, J. E., Newhouse, M. L., and Elliott, P. M., *British Medical Journal*, 1966, 1, 409.
- ⁴ Flynn, C. A., and Gardner, F., *British Journal of Medical Education*, 1968, 3, 28.
- ⁵ *British Medical Journal*, 1976, 1, 188.
- ⁶ Clark, P. A., in press.
- ⁷ Department of Health and Social Security, *Re-employment of Women Doctors*, HM(69)6. London, DHSS, 1969.
- ⁸ Department of Health and Social Security, *Women Doctor's Retainer Scheme*, HM(72)42. London, DHSS, 1972.
- ⁹ Ministry of Health, *Special Scheme for Postgraduate Education for Doctors who wish to return to Medicine as General Practitioners after an Absence*, ECN 544. London, Ministry of Health, 1966.
- ¹⁰ *British Medical Journal*, 1976, 1, 56.
- ¹¹ *BMA News Review*, 1976, 1, 1.
- ¹² Essex-Lopresti, M., *Lancet*, 1970, 2, 204.
- ¹³ Rue, R., *Lancet*, 1967, 1, 1267.
- ¹⁴ Arie, T., *British Medical Journal*, 1975, 3, 641.

Hospital Topics

Use of creatine kinase for detecting severe X-linked muscular dystrophy carriers

N R DENNIS, K EVANS, B CLAYTON, C O CARTER

British Medical Journal, 1976, 2, 577-579

Summary

Women thought to be at risk of being carriers of Duchenne

MRC Clinical Genetics Unit, Institute of Child Health, London WC1N 1EH

N R DENNIS, MB, MRCP, scientific officer

K EVANS, AIMSW, medical social worker

C O CARTER, DM, FRCP, professor of clinical genetics and director

Institute of Child Health and the Hospital for Sick Children, London WC1

B CLAYTON, MD, MRCPATH, professor of chemical pathology

muscular dystrophy were given "odds" against their having an affected child. These were calculated from a combination of the genetic risk from the family history and an estimation of the biochemical risk from measuring the serum creatine kinase concentration. The women were told the actual risk estimate and it was put into perspective for them as a high, medium, or low risk. Of 25 women at high risk six have had children, all girls; the two in the medium-risk group have had no children; and the 46 women at low risk have had 19 boys and 25 girls. None of the boys has the disease.

With detailed counselling most potential carriers of this disease reach decisions in child bearing that are in line with their degree of risk.

Introduction

In 1960 Schapira *et al*¹ reported raised creatine kinase (CPK) activity in the serum of female carriers of the severe X-linked (Duchenne) form of muscular dystrophy. Hughes² and Rich-terich *et al*³ plotted frequency distributions of CPK levels in controls and carriers and suggested that these might help in genetic counselling. Although the range of activity among the carriers overlaps with that in female controls, CPK estimation is generally regarded as the most reliable means of identifying carriers among women with a high genetic risk.

At the genetic clinic at the Hospital for Sick Children we have had 10 years' experience of the test. We have checked the accuracy of the assignments in two ways. In 103 women who were possible carriers we compared the odds given by the biochemical test with the genetic odds estimated from the pedigree, and we followed up the 73 women aged 18-40 years to see if their sons were affected. None of the women were obligatory carriers—that is, women with an affected son and at least one other affected male relative. The CPK levels of the obligatory carriers tested since 1965, however, provided a check on the original distribution of CPK levels in carriers (see below).

Patients and methods

Of the 103 women, 96 were seen at the genetic clinic at the Hospital for Sick Children and seven at the genetic clinic at Oxford. In every case the CPK value used was the mean of three measurements taken at roughly weekly intervals, and all estimations were made in the chemical pathology laboratory of the Hospital for Sick Children by Hughes's method.⁴ The results are expressed as μmol creatine liberated/ml of serum/hour at 37°C, creatine being determined colorimetrically. The women were advised to avoid sustained heavy exercise for 24 hours and to rest for 30 minutes before each test; otherwise they followed their normal activities. No attempt was made to standardise the time of day when the specimens were taken, except that most were taken two to three hours after the last meal to avoid lipaemia. Blood was usually taken at their first attendance at the clinic, and two further specimens were obtained later. Some of the women returned to the clinic for the second and third specimens; others

TABLE I—CPK levels in second series of 15 controls and 15 known carriers (each value is mean of three estimations)

Controls	1.27, 0.92, 0.82, 0.94, 1.85, 1.14, 1.12, 1.09, 1.27, 1.22, 0.93, 2.27, 1.77, 1.43, 1.20
Carriers	2.8, 11.9, 3.6, 5.2, 1.43, 2.1, 2.3, 2.0, 10.2, 4.2, 2.5, 16.9, 3.0, 3.3, 8.9

Mean (SD) of log values—Controls: 0.0907 (0.1228). Carriers: 0.6092 (0.3197).

TABLE II—Comparison of genetic and biochemical odds

Biochemical odds	Genetic odds				Total
	2:1	1:1	1:2	<1:2	
>1:1	4	19	3	10	36
<1:1	2	19	16	30	67
Total	6	38	19	40	103

TABLE III—Pregnancies and related decisions of 73 women who underwent CPK estimation

Risk	Children born				Couples planning more children	Since CPK		
	before CPK		after CPK			Termination	Sterilisation	
	Boys	Girls	Boys	Girls			Husband	Woman
High (n = 25)	4 (1A)	7		6 (3 FS)	7 (all FS)	4†	1	6
Moderate (n = 2)		2						
Low (n = 46)	5 (1A)	9	19*	25	12 (1 FS)	1†	1	2

*CPK levels estimated. †Unplanned pregnancies.
A = Affected with muscular dystrophy. FS = Fetal sexing.

attended their local hospital or general practitioner's surgery, where the serum was separated from a 2-5 ml blood sample according to our instructions and then posted. Plasma or serum specimens sent by post are satisfactory provided there has been no haemolysis before separation.

ESTIMATION OF ODDS

Use of CPK values to provide a quantitative estimate of the odds against a woman being a carrier has been described by Wilson *et al*⁵ and Emery.⁶ We used results reported by Wilson *et al*⁵ in 17 carriers and 21 controls, later augmented by a more recent series of our own of 15 carriers and 15 controls (table I) to prepare distribution curves of the logarithms of the CPK serum concentrations in the two groups. An individual woman's risk of being a carrier could then be estimated by comparing her CPK serum concentration with the carrier and control curves (we assumed that the log values were normally distributed in each group).

GENETIC ODDS

The genetic odds were calculated from the pedigree by Bayes's theorem,^{7,8} assuming equal mutation rates in the two sexes, and were multiplied by the biochemical odds to give an overall figure.

Results

COMPARISON BETWEEN GENETIC ODDS AND CPK FINDINGS

A CPK level of 2.03 corresponds to biochemical odds of 1:1. Table II shows the number of women falling above and below this level in the various genetic odds categories. For this purpose the genetic odds were calculated solely on the basis of pedigree information, ignoring any CPK values available in other members of the family. The correspondence between the genetic odds and the distribution of biochemical odds (table II) was reasonably close. By chance it was perfect for genetic odds of 2:1 and 1:1. There was an excess of biochemical odds of less than 1:1 in the genetic 1:2 category and a deficit in the genetic <1:2 category since this included no women with odds greater than 1:3 (the average value being about 1:6), but neither difference was statistically significant.

The biochemical odds for some of the women were worked out when they were first seen from estimation of the individual CPK value and calculation of the probability of finding that value or less in a carrier to the probability of finding that CPK value or more in a control. This method was slightly erroneous, and it overestimated the probability of a woman's being a carrier; but when the odds were recalculated using the correct method, comparing the height of the ordinates at that value, the change was found to make very little difference to the three broad risk categories to which patients had been assigned. The women knew that only males were affected so that risk could be expressed as 1 in *n* for an affected son or 1 in 2*n* for an affected child. All the women had been given an actual estimated risk, account being taken of CPK values in other family members—for example, the mothers of those who had been tested. Thus a woman with an affected first cousin might at first sight have a low genetic risk, but if her mother was found to have an unequivocally high CPK level her odds would be increased to 1:1.

We divided the women into three groups according to the risk they were given at the time of counselling: the high-risk group consisted of women whose odds of being a carrier were 1:2 or greater, corresponding to a 1 in 12 or greater risk of an affected child; the moderate-risk group consisted of women with odds from 1:2 to 1:10, corresponding to a

risk of between 1 in 12 and 1 in 44; and the low-risk group included women whose odds were less than 1:10, with a risk to a child of less than 1 in 44. (If our later method had been used in estimating the biochemical odds four women originally allocated to the high-risk group would have been in the moderate-risk group, and one originally allocated to the low-risk group would have had a moderate risk.)

FOLLOW-UP

The children born to the three groups of women before and after testing and the women's response to genetic counselling are shown in table III.

The 25 women in the high-risk group bore no sons, but six girls were born—three of them after fetal sexing. No children were born to the two women in the moderate-risk group. The low-risk group of 46 women bore 19 sons and 25 daughters after they were tested. All 19 sons had a CPK test; none of the values were abnormal and no boy developed the disease.

In the high-risk group seven women said they were planning further pregnancies, but all intended to undergo fetal sexing and termination if the fetus was male; 16 women were not planning further children, and two were uncertain (one of these was not yet married). Of the 16 planning no more children four had had unplanned pregnancies terminated, and six women and the husband of a seventh were, at their own request, sterilised.

One of the women at moderate risk, who already had two girls, was planning no more children, and her husband has been sterilised. The other was not yet married and was undecided.

In the low-risk group at least 12 women wanted more children (one intended to have fetal sexing); one woman had an unplanned pregnancy terminated and two others were sterilised (one for gynaecological reasons and the other after having three children because she felt her family was complete).

Discussion

The genetic and biochemical odds compared well, and no affected boy has yet been born to any of the 73 fertile women tested. The understandable family planning decisions of the women given a high risk precludes a prospective check on the risk estimates for this group. Similarly, in Emery's⁹ high-risk group (greater than 1:4 of being a carrier) only two of the 41 women planned a child, and fortunately both children were unaffected. The fact that 19 sons, all unaffected, were born to women with a low risk (odds less than 1:10 of being to not being a carrier) is encouraging. Only five of these sons, however, were born to women with the high genetic odds of 1:1 before CPK testing. Three women in this group had a termination before testing, a procedure which they would probably not have requested if they had been tested earlier.

The decisions of these women and their husbands after genetic counselling and, often, discussion with their family doctors shows how serious they regard a high or moderate risk of the disorder. Most of these women were familiar with the course of the disease in a brother or cousin, and two had already had an affected son. The only woman who planned children with little regard to the risk was one who was tested at 14 and, regrettably, had not attended the clinic since. Fortunately both her children were daughters. Emery *et al.*⁹ reported that a high-risk estimate had an equally strong deterrent effect. His study, however, included obligatory carriers and a majority of women who had had at least one affected child. In our follow-up sample only two women, one at high-risk and one at low-risk, had already had an affected child. There is clearly growing interest in the availability of fetal sexing and termination of the pregnancy if the fetus is male. The possibility needs to be discussed when a couple request sterilisation. There is evidence¹⁰ that CPK estimations during pregnancy are not reliable. We do not usually test girls until they are 17 or 18 years old. If seen earlier we recommend to the parents that the girls attend the clinic again, preferably with their fiancés before marriage.

The low-risk group were almost all sufficiently reassured to be able to consider pregnancies. Even if an affected boy had been

born to a woman in this group, this tragedy would have to be evaluated against the 43 other unaffected children, most of whom would not have been born without the reassurance of the low-risk estimate. Emery *et al.*⁹ report three normal sons born to the seven women with a low risk (risk less than 1:9 of being a carrier). Two women in our group, however, still felt the risk was unacceptable; one plans no children and the other plans another pregnancy, but wants it to go to term only if the fetus is female. A third woman whose family is complete and has an affected son also says she has not found the test sufficiently reassuring. Similarly, one of Emery's⁹ low-risk group was not reassured and planned no children.

The results we report are encouraging, but there is much scope for improvement. A larger series of controls and obligatory carriers would make clearer the actual distribution of CPK values in both. There are many different methods of measuring CPK, and it is important that any laboratory offering the service should establish its own distributions and not rely on those published by others. Full details of our own figures and methods are available on request. While precise detection of carriers will perhaps not come until the biochemical defect in the disease is discovered, development of any further discriminatory tests, if independent of CPK values, will be valuable and can be incorporated into the risk estimate.

We are most grateful to Mrs J Warren, who visited most of the families in the follow-up study; to the technical staff of the department of chemical pathology at the Hospital for Sick Children; to Dr R H Lindenbaum, who allowed us to include the families from Oxford; and to Dr J Renwick, who a few years ago drew our attention to the earlier error in calculating the biochemical odds.

References

- Schapiro, F, *et al*, *Revue Francaise d'Études Cliniques et Biologiques*, 1960, **5**, 990.
- Hughes, B P, *British Medical Journal*, 1962, **2**, 963.
- Richterich, R, *et al*, *American Journal of Human Genetics*, 1963, **15**, 133.
- Hughes, B P, *Clinica Chimica Acta*, 1962, **7**, 597.
- Wilson, K M, Evans, K A, and Carter, C O, *British Medical Journal*, 1965, **1**, 750.
- Emery, A E H, *Journal of the Neurological Sciences*, 1969, **8**, 579.
- Murphy, E A, and Mutalik, G S, *Human Heredity*, 1969, **19**, 126.
- Stevenson, A C, and Davison, B C G, *Genetic Counselling*, p 72. London, Heinemann, 1970.
- Emery, A E H, Watt, M S, and Clack, E R, *Clinical Genetics*, 1972, **3**, 147.
- Blyth, H, and Hughes, B P, *Lancet*, 1971, **1**, 855.

A patient with recurrent threadworm infections has been treated with pyriminium pamoate (Vanthin) and piperazine and at times other members of the family have been treated concurrently. Are these recurrences likely to be repeated reinfections or a failure of treatment? Can threadworms give rise to any allergic symptoms referable to the bowel or more general ones?

Pyriminium pamoate (a single dose of 5 mg/kg body weight) or piperazine adipate (Antepar) (9 mg/kg body weight daily for seven days) should cure over 90% of the people treated. Even when the entire family is treated simultaneously reinfection is likely because the eggs remain viable in clothes, underwear, dust, and lavatories—not only in the house but also in school. Eradication is impossible even though complete cure may be achieved by repeated treatment.¹ The commonest symptoms are pruritus, which is probably an allergic symptom, and it is usually localised to the anus and vulval region. More generalised reactions may occur in atopic individuals, and eosinophilia may be a feature of the infection. Threadworms are often found in the appendix, usually as an incidental finding, but they may give rise to inflammatory lesions resulting in appendicitis. A more detailed account of this infection is in *Worms and Disease*.²

¹ Matsen, J M, and Turner, J A, *American Journal of Diseases of Children*, 1969, **4**, 576.

² Muller, R, *Worms and Disease*, p 161. London, William Heinemann, 1975.