fact, this relatively narrow weight band which Frisch has identified as being associated with most female menarches.—ED., *B.M.J.*

1 Frisch, R. E., Revelle, R., and Cook, S., *Science*, 1971, **174**, 1148.
2 Frisch, R. E., in *Control of the Onset of Puberty*, ed. M. M. Grumbach, G. D. Grave, and F. E. Mayer. New York, Wiley, 1974.

SIR,—Certain statements in your leading article on this subject (12 April, p. 52) may be misleading and require clarification. We believe that on the evidence presented it should not be concluded that a weight-dependent differential response to luteinizing hormone, follicle-stimulating hormone, releasing hormone (L.H./F.S.H./R.H.) exists which will distinguish anorectics from other women *of similar weight* with secondary "functional" amenorrhoea.

You state that "it has been found that the hormonal responses to L.H./F.S.H./R.H. are particularly dependent on body weight. When patients treated with normal diet (but not ambulant) were studied it became clear that there is a weight threshold of close to 45 kg. Below this weight gonadotrophic responses to the releasing hormone were restricted. . . ." It is important to appreciate that the reference quoted[1] referred not to normal patients but to patients with anorexia nervosa. We could find no comment about the weights of normal patients investigated by Besser *et al.*[2] Nor was reference made to any comparable study of normal patients who were below 45 kg body weight.

Your article goes on to say that "Other workers,[3 2] however, studying anorectic patients but using twice the amount of releasing hormone (100 μg instead of 50 μg) as a stimulus found that pituitary responsivity was adequate. Apparently the pituitary is capable of releasing L.H. and F.S.H. at low weights but it requires a greater stimulus." Though this may be true, in our opinion the references quoted in support of this view have been misinterpreted. In the paper by Mortimer *et al.*[3] an adequate response obtained by administering various doses of L.H./F.S.H./R.H. to *normal* patients was reported but we could find no mention of the effect in anorexia nervosa nor of the patients' body weights. In the paper by Mortimer *et al.*[3] an adequate response to 100 μg of L.H./F.S.H./R.H. was demonstrated in 11 out of 13 anorectics, but again they made no mention of the patients' body weights. While these patients may have weighed less than 45 kg, we feel that this is an unjustifiable assumption. It should not be assumed that anorectic patients of low body weight would necessarily respond to a 100-μg dose of L.H./F.S.H./R.H.

Furthermore, Akande *et al.*,[4] whose work is quoted, studied the effect of 25-100 μg of L.H./F.S.H./R.H. in eight amenorrhoic women *whose weights were not stated.* If, as seems likely, body weight is an important factor in determining the response to L.H./F.S.H./R.H. it is possible that low-weight patients with "functional" amenorrhoea may also have a poor response to a 50-μg dose of L.H./F.S.H./R.H.—We are, etc.,

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1 Palmer, R. L., *et al.*, *British Medical Journal*, 1975, **1**, 179.
2 Besser, G. M., *et al.*, *British Medical Journal*, 1972, **3**, 267.
3 Mortimer, C. H., *et al.*, *British Medical Journal*, 1973, **4**, 73.
4 Akande, E. O., *et al.*, *Lancet*, 1972, **2**, 112.

Serum α-Fetoprotein in Cystic Fibrosis

SIR,—The recent article by Professor R. K. Chandra and his colleagues (29 March, p. 714) concerning elevated levels of α-fetoprotein (AFP) in the serum of patients with cystic fibrosis and their relatives is of great interest. Over the past 12 months we have examined by both counterimmunoelectrophoresis and radioimmunoassay sera from (*a*) 37 patients with cystic fibrosis (age 6 months to 17 years), (*b*) 10 of their siblings, and (*c*) 24 of their parents for the presence of raised serum levels of AFP. The controls included sera from adults and children without a history of cystic fibrosis as well as sera from 62 patients with a variety of hepatic diseases, including hepatoma, jaundice, and hepatitis.

The accompanying table gives a summary of our findings and shows that by counter-immunoelectrophoresis we were unable to detect an increased serum concentration of AFP in any of the cystic fibrosis patients or their relatives. The limit of detection of

	Serum AFP			
	Counterimmuno-electrophoresis		Radio-immunoassay	
	No. Examined	Detection	No. Examined	Median values (μg/l)
Patients with cystic fibrosis	37	0	24	10
Heterozygotes	24	0	9	10
Siblings	10	0	2	10
Positive controls	62	8	62	>128
Negative controls	30	0	15	10

AFP by counterimmunoelectrophoresis in our laboratory is about 100 μg/l. The majority of the positive control patients with hepatoma who had serum AFP concentrations above 128 μg/l gave a positive AFP immunoprecipitin line by the counter-immunoelectrophoretic method, but no such immunoprecipitin lines were detectable in any of the sera from the cystic fibrosis patients. In addition, the results from the radioimmunoassay method showed that all of the cystic fibrosis patients and their relatives had normal concentrations of AFP in their serum. The median values obtained for serum AFP concentrations by radio-immunoassay in all the cystic fibrosis patients and their relatives whom we tested was 10 μg/l. The upper limit of the normal value of serum AFP concentration is 25 μg/l. —We are, etc.,

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SIR,—Dr. R. K. Chandra and his colleagues (29 March, p. 714) report values of serum α-fetoprotein (AFP) which were greatly elevated in children with cystic fibrosis of the pancreas (56-8825 μg/l; normal range 5-25 μg/l). They also found no overlap between the serum AFP levels of the parents (25-568 μg/l), who are presumed heterozygotes, and those of healthy controls. This suggests a promising new method of diagnosing the disorder and even identifying those at risk of having affected children.

We have not been able to confirm these findings. Using a double antibody radioimmunoassay[1] we found the mean serum AFP for seven children with cystic fibrosis to be little different from that of controls (see table), while all seven values fell within the normal range for this series and also for those of Dr. Chandra and his colleagues and of Ruoslahti and Seppala.[2] We are unable to

	No. of Subjects	Serum AFP (μg/l)	
		Range	Mean and S.D.
Cystic fibrosis	7	2·0-9·25	6·3 ± 2·5
Controls	10	3·4-18·0	8·2 ± 5·2

explain this discrepancy, for, though the assay used by Dr. Chandra and his colleagues is inadequately described, they appear to be using the same rabbit antiserum and standards as ourselves.—We are, etc.,

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1 Brock, D. J. H., Bolton, A. E., and Scrimgeour, J. B., *Lancet*, 1974, **1**, 767.
2 Ruoslahti, E., and Seppala, M., *Nature*, 1972, **235**, 161.

SIR,—The report by Professor R. K. Chandra and others (29 March, p. 714) makes very interesting reading. I would like to confirm their findings and support the hypothesis they are proposing. In seven patients considered to have cystic fibrosis on the basis of a sweat chloride level above 65 mmol/l the mean serum α-fetoprotein (AFP) level was 1825 (range 130-2360) μg/l. The corresponding level in the parents was 433 (range 80-1055) μg/l. Three out of 11 siblings showed elevation of AFP concentration, the figures being 840, 1365, and 1980 μg/l respectively.

There are three additional points to be made. Drug therapy given to these patients may have a subtle hepatotoxic influence, thereby causing a rise in AFP levels. The severity of the disease does not influence the degree of elevation. There is a corresponding rise in carcinoembryonic antigen levels also, but the latter is related to the degree of tissue damage and results from the sero-cross-reactivity between mucus-producing respiratory mucosa and fetal tissues.

If confirmed by other workers, these data would have considerable relevance to genetic counselling and primary prevention of the disease.—I am, etc.,

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