VITAMINS AND PHYSIOLOGICAL FUNCTION

BY

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A report has recently appeared from Manchester University of some observations in which a short period of supplementary feeding with vitamins produced significant changes in physiological function (Harper, Mackay, Raper, and Camm, 1943). The supplement, consisting of 6,000 I.U. vitamin A, 1,000 I.U. vitamin D, and 50 mg. vitamin C daily, was given to 35 cadets aged 18 to 19 for a period of 10 weeks, while 34 cadets received control pellets and capsules. At the end of 10 weeks the groups were changed over, so that the control group now received the vitamins for 11 weeks. The cadets had recently joined the Forces; during their training they were receiving, at the University refectory, a diet similar to that of the undergraduates. It was found that the group receiving the vitamins were superior in several respects to the control group: the vital capacity, breath-holding time, endurance (R.A.F. 40-mm. mercury test), and, surprisingly, the resting pulse rate, were all considerably increased in the vitamin-fed group. In addition there was a significant difference in the number of days during which the cadets complained of minor respiratory or gastro-intestinal disorders, those receiving the pellets having on the average 9.7 days of complaints per man, compared with 14.9 days per man in the control group. On the other hand, no difference was found in height, weight, chest girth, or pelvic measurement, nor in the standing pulse rate, the pulse rate during the R.A.F. endurance test, the post-exercise pulse rate, or the post-exercise vital capacity.

As it happened that elementary-school children were available in Cambridge who, in the course of other investigations, had been receiving vitamin pellets for a year, it seemed that the opportunity might usefully be taken to examine the general applicability of the findings of the Manchester investigators. To this end we have repeated the tests on the four functions which these workers found to be affected.

The vital capacity was measured after the heart rate had been taken. It was found that the first one or two attempts were usually lower than subsequent attempts. Readings were therefore made until fairly consistent results were obtained, and the highest of these was taken as the true vital capacity; five or six attempts were usually sufficient. Owing to the variation in heights and weights of the children the vital capacity has been divided by the surface area in order to obtain a truer comparison.

Breath-holding was the time in seconds during which the subject could hold his breath after full inspiration, and the endurance test the time in seconds during which the subject could maintain, after full inspiration, a column of mercury at a height of 40 mm.

Half of the 12-year-old boys were examined three days after the completion of a vitamin C saturation test, during which they each received 70 mg. vitamin C daily per stone body weight (i.e., some 350 mg. daily on the average) for 5 successive days. A comparison was made of these 38 boys with the 38 who were not given the saturation test (Table I). (It might be

TABLE I.—Effect of Saturation with Vitamin C on Physiological Function

	Boys Receiving Vitamin Pellets		Boys Receiving Control Pellets	
	Saturated	Not Saturated	Saturated	Not Saturated
Number examined	19	19	15	23
Average resting pulse rate (beats per min.)	82.2	83.8	77	82
Average vital capacity (ml.)	2,310	2,142	2,297	2,145
Average vital capacity/sq. metre body surface	1,862	1,710	1,840	1,770
Average breath-holding time (secs.)	39.0	41.7	36.4	35.4
Average endurance test (secs.)	27.2	25.8	26.4	23.1

mentioned that all the boys subjected to the saturation test became saturated within the five days of the test, the majority within the first two days.) It will be seen that the differences between the "saturated" and "unsaturated" boys were in each case very small, and statistical treatment is hardly necessary to demonstrate that these differences are insignificant. We have nevertheless subjected some of the bigger differences to statistical analysis—for example, the apparent higher vital capacity in the "saturated" boys—and in each case the difference is not significant. This was also true when the "vitamin" group and the control group were combined.

TABLE II.—Effect of Vitamin Supplements on Physiological Function

	Boys, 12 Years Old		Boys, 11 Years Old		Total Boys		Girls		Total Subjects	
	Vitamin Group	Control Group	Vitamin Group	Control Group	Vitamin Group	Control Group	Vitamin Group	Control Group	Vitamin Group	Control Group
Number examined	38	38	10	12	48	50	39	41	87	91
Average resting pulse rate (beats per min.)	83	77.6	86.8	90.4	83.6	80.8	88.2	87.8	85.8	85.4
Average vital capacity (ml.)	2,213	2,200	2,010	2,164	2,185	2,196	1,916	2,064	2,064	2,135
Average vital capacity/sq. metre body surface	1,792	1,800	*	*	1,770	1,818	1,638	1,600	1,690	1,712
Average breath-holding time (secs.)	40.4	35.8	34.8	39.7	39.3	36.4	34.2	32.2	37.0	34.5
Average endurance test (secs.)	26.4	23.9	22.8	25.0	25.7	24.5	18.7	21.1	22.8	23.1

* Surface area not available for all subjects.

Experimental

Altogether 178 children have been examined; these comprised 80 12-year-old girls, 76 12-year-old boys, and 22 11-year-old boys. About half in each group—alternate children from the school register—had received vitamin pellets daily at school and the remainder control pellets. The vitamin pellets contained 5,000 I.U. vitamin A, 1 mg. vitamin B₁, 25 mg. vitamin C, and 500 I.U. vitamin D. The children were living and eating at their homes, except for some who had dinner at school. Allowing for week-ends and holidays, the average supplement over the year was roughly half the reputed daily requirements of these nutrients; apart from the vitamin B₁, which Harper *et al.* did not administer, the children were thus obtaining less of the supplemented vitamins than the subjects at Manchester.

The heart rate was measured over a half-minute period after the children had been sitting quietly and comfortably for 15 minutes, and again after a further 5 minutes. Preliminary tests had shown that this procedure gave much more consistent results than measurements taken with the children lying down.

We can therefore consider the "saturated" and "unsaturated" boys together, and compare those who had received the vitamin supplements with those who had not. Table II shows this comparison, together with the girls and the 11-year-old boys; none of the girls or the 11-year-old boys had been subjected to the vitamin C saturation test before the examination for physiological function.

It is evident from simple inspection that no significant difference exists between the subjects receiving the vitamin supplements and the controls. Such small differences as occur are often in opposite directions; thus the boys on the vitamin pellets have an average vital capacity, expressed as a function of their surface area, of 48 ml. less than that of the control group of boys; in the girls the value of the "vitamin" group is 38 ml. more than the control group. Also, considering all the children, whereas the average breath-holding time is higher in the vitamin group, the average vital capacity and the endurance time are slightly lower. Again statistical analysis confirms that none of the differences are significant.

Discussion

The Manchester workers have themselves pointed out some possible criticisms to which their results might be open. In particular, they refer to the small number of their subjects. Additional queries arise even although their results are statistically outside the limits normally accepted for chance variations (see Abrahams, 1943; also *British Medical Journal*, 1943).

If, however, we accept the validity of the findings of these workers, the fact that vitamin supplements did not induce such changes in physiological function in our subjects might possibly be due to their not having been deficient in these nutrients before the administration began. This is supported by the fact that there was also no improvement in other respects after the year's dosing (see Yudkin, 1943). Gain in height and weight, strength of grip, haemoglobin, intelligence, educational attainment, and dark-adaptation were no different in those children receiving the supplement from what they were in those receiving the control pellets. Moreover, although there was a reduction in the incidence and duration of colds in the vitamin group, this was seen only in the younger children and was not shown by the older children examined for physiological function.

It should be emphasized that the absence of effect in our subjects may be due to differences in age or in degree of deficiency; they are not therefore to be interpreted as contradicting the findings of Harper *et al.* Nevertheless it is clear that improvement of physical efficiency by vitamin supplements cannot be regarded as being generally applicable to all groups.

Summary

A group of 178 children aged 11 and 12 were examined after about half of them had received vitamin supplements daily at school for one year. The supplements provided each school day 5,000 I.U. vitamin A, 1 mg. vitamin B₁, 25 mg. vitamin C, and 500 I.U. vitamin D, the average addition over the year being about one-half of the reputed daily requirements of these substances.

No difference was observed between the control group and the supplemented groups in resting pulse rate, vital capacity, breath-holding, or 40-mm. endurance test.

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THE CRY OF THE CHILD IN UTERO

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"Vagitus uterinus" is the term applied to the crying of the child while its head is still in the uterus. Mohammed and St. Bartholomew are both supposed to have made themselves heard *in utero*. It may be of importance in medico-legal cases, as it is possible in this way for a child to be stillborn and yet have its lungs partly aerated. In some cases this cry of the child may also be a warning of foetal asphyxia, requiring a rapid delivery.

Record of a Recent Case

Mrs. T., a primigravida aged 29, was sent up to the London Hospital at 40 weeks with a breech presentation. External version under anaesthesia failed and she came into labour spontaneously two days afterwards. The membranes ruptured after 27 hours with the cervix fully dilated, and 1½ hours later it was decided to assist delivery as the anterior buttock had been peeping without advance for half an hour and the mother was becoming distressed. The foetal heart rate was 160 a minute. The resident accoucheur performed a postero-lateral episiotomy under gas, oxygen, and ether, with the patient in the lithotomy position, but was unable to bring down a leg as there was little liquor. The registrar therefore took over, and just as he was passing his hand gently up the vagina the foetus was felt to give a convulsive movement and everyone in the labour theatre heard a "foetal cry." This was repeated twice more, and was accompanied by movement of the foetus. The cry was

loud, and was heard by three doctors, two hospital sisters, and three nurses; and all this when the anterior buttock was just peeping at the vulva. Rapid delivery was performed, bringing down the legs and arms, and forceps was applied to the after-coming head. Although this was done quickly the foetus was making strong inspiratory efforts during delivery. The female infant of 6 lb. 6 oz. was very cyanosed, but breathed at once and recovered rapidly.

Discussion

For this condition to occur it is necessary for air to be present in the uterus. This may be due to the suction of air along the examining hand during the relaxation of the uterus, as probably occurred in this case. If the patient had been delivered on the left side there would have been a tendency for gravity to pull the foetus and uterus out of the pelvis and so suck air into the vagina or even the uterus. Miss Field at the meeting of the Obstetric Section of the Royal Society of Medicine on March 19, 1943, described a case in which air rushed up the catheter during high rupture of the membranes and was followed by foetal crying, and 54 hours later by the delivery of a living child. Mr. Fraser's case at the same meeting was harder to understand. A 4-gravida, 30 weeks pregnant, ruptured her membranes five days before delivery. Twenty-four hours before delivery the foetus was heard to cry *in utero* for 40 minutes with the os only one-fifth dilated. Tympanites and succussion splash were present. The premature foetus died with a cerebral haemorrhage three hours after delivery. Air was perhaps sucked into the uterus during a uterine relaxation, or by the piston-like action of the foetal head. Although afebrile there may have been a low-grade infection with gas-forming organisms.

Once there is air in the uterus the foetus must inspire in order to produce a cry. There are at least two types of intra-uterine cry. The first is a soft whimpering cry—best heard with a stethoscope to the abdomen—which may continue for a considerable time and is not associated with asphyxia of the infant. This was the type of cry in the latter two cases. The second type was found in our case, in which the cry was loud and gasping, and was accompanied by a convulsive movement of the foetus and associated with foetal asphyxia.

The work of Barcroft and Barron on the respiratory centre of lambs *in utero* throws light on this problem. The movements responsible for respiration can be traced back to the first efforts that the foetus makes, and it seems that a third of the way through pregnancy the essential neuro-muscular mechanism has been laid down and as it were tried out. At first the respiratory movements occur as a reflex to a stimulus. This becomes more sensitive and the response more differentiated, but, later, with the development of the controlling higher nervous centres the foetus again becomes inert. With the onset of labour there is a degree of anoxaemia which depresses the inhibiting higher centres, so that the foetus shows more movement. There is also an increase of CO₂ pressure, and an avalanche of sensory impulses which all have a large stimulating effect on respiration.

In the first group there is a gentle whimpering cry which is unassociated with asphyxia and occurs before or early in labour. This noise is due to air passing in and out of the chest, whereas normally there is a tidal flow of liquor. In these cases the foetus can be stimulated by prodding, when the cry may be louder. In the second group the type of respiration is gasping, is associated with foetal asphyxia, and occurs when labour is well advanced. It has been shown by Barcroft that transection of the brain-stem above the level of the hypoglossal nucleus in the sheep foetus causes this form of respiration, and it is suggested that this gasping type of cry in the human foetus is due to anoxaemia of the higher nervous centres releasing the lower medulla.

Yet another possibility is that once there is air in the body of the uterus it may be suddenly forced past a fold of membrane or vagina by a contraction of the uterus. A noise simulating a foetal cry might thus be produced. Sipple's case was quoted in the *British Medical Journal* of Sept. 14, 1912. While carrying out an internal version he had to hold his hand still during a contraction. At that moment there were two high-pitched noises just like an infant's cry, but he noticed that they were accompanied by a sensation of air running up his forearm.