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Follow-up Examination of Children Exposed to Ultrasound in Utero

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Follow-up examinations were carried out in 171 children ranging in age from 6 months to 3 years, who had been exposed to ultrasound in utero. One third of the children were born from pathologic pregnancies. About 50% of the mothers had been subjected to ultrasound examination in a single instance, while more than four such examinations were carried out in 30 cases, mostly after the 31st week of pregnancy.

Physical and mental development of the examined children corresponded to the standard values for the general population. The examined material contained two cases of mild congenital cardiopathy, two cases of coxal dysplasia and one case of inguinal hernia. These figures compare closely with the general average.

Chromosomal examinations were carried out in 10 randomly selected children exposed to ultrasound and 10 controls. Two chromosome aberrations were encountered; the incidence was non-significant statistically. Thus, ultrasound exposure of pregnant women does not seem to give rise to congenital malformations and chromosomal aberrations in the foetus.

Ultrasound is being increasingly adopted as a diagnostic tool in obstetric practice, and its still wider use is predictable [7, 8, 22]. The method has become practically indispensable for the demonstration of early pregnancy, of intrauterine death, threatening abortion, molar pregnancy, further for the point of placental attachment [18]. In all these cases the foetus is exposed to ultrasound.

Numerous as the advantages of ultrasonic examination are, investigators have long been attempting to determine its eventual harmful effect [1, 2, 4, 6, 9 to 15]. It was, however, proved by laboratory studies and animal experiments [21, 23, 24, 25] that diagnostic ultrasound is harmless for the mother as well as for her offspring including the latter's development and chromosomal conditions. The findings of MacIntosh and Davey [16] in 1970 were, therefore, surprising. Relying on the evidence of experiments in vitro, they pointed to the dangers of ultrasound. It should, however, be noted that these authors treated leucocyte cultures with ultrasound for 1—2 hrs in an aphysiological manner. It was in these circumstances that they observed chromosome breaks and other aberrations which induced them to assume that the routine application of ultrasound may entail chromosomal

damage. SERR et al. [20] in 1970 reported that out of ten cases of late abortion in which the pregnant women had been subjected to ultrasonic examination, two of the aborted foetuses displayed a pathologically high number of broken chromosomes. These papers created a great stir and a number of investigators instituted experiments which, while similar to those described above, were carried out under considerably more physiological conditions. None of them was able to confirm the dangerousness of ultrasound [17, 19].

After such antecedents we, too, felt impelled to examine children in in the first postnatal years who had been exposed to ultrasound in utero. In doing so we were led by the conviction that, apart from in vitro and animal experiments, human follow-up examinations were of prime importance.

MATERIAL AND METHOD

It was in 400 obstetrical cases that between 1967 and 1970 ultrasound examinations had been performed in Korvin Hospital. The Kretz-Technik 4100 MGS type of apparatus was employed with the usual intensity of 0.001—0.004 W/cm². All in all, 171 children were brought for follow-up examination; the rest seemed to have left the town, while some parents remained indifferent. It was mostly in the case of perfectly healthy children that the parents deemed the examination unnecessary.

TABLE I

Distribution of material according to manner of delivery

Spontaneous	123
Vacuum extraction	15
Caesarean section	33
Total	171

We investigated all details of the cases including psycho-social conditions. In addition to the usual paediatric examinations we determined the children's weight, body length and head circumference. If necessary, cardiological, ophthalmological, otological, orthopaedic and laboratory studies were done.

Chromosomal examination was carried out in 10 cases selected at random and in 10 age-matched children not exposed to ultrasound. Table I shows the distribution of the examined children according to the manner of delivery. More than one third was born under pathologic conditions; the frequency is explained by the fact that ultrasound examination had mostly been applied in cases of pathological pregnancy.

It can be seen from Table II that in the majority a single ultrasonic examination was made and only in 30 cases were more than four such examinations carried out.

The phase of pregnancy in which the examination is made seems to be important with regard to complications. As seen in Table III, in 10 cases only was ultrasound applied in the first three months of gesta-

TABLE II

Number of ultrasound examinations

Number of examinations	1	2—3	4—6	7<	Total
Number of children	84	57	26	4	171

TABLE III

Time of ultrasound examinations

Week of pregnancy	8—12	13—20	21—30	31<
Number of examinations	10	24	75	259

tion; most examinations were made after the 31st week.

Distribution of the children according to birth weight and duration of pregnancy is presented in Table IV. There were few neonates with low birth weight in the material. This was due to that in numerous cases prolonged labour or disproportion between foetal head and maternal pelvis was the reason for the ultrasound examination.

The age of the children at the time of the follow-up ranged from 2 to 3 years in 34 cases, from 1 to 2 years in 69 cases, from 6 months to 1 year in 68 cases.

RESULTS

The anthropometric chart of Boston University was used for the representation of body weight and body length (boys in Fig. 1, girls in Fig. 2). Each dot in the diagrams represents a separate individual.

It can be seen that body weight and longitudinal growth were, in the overwhelming majority, between 10 and 90 percentile (with considerably more values over 50 percentile).

In general, both the alimentary and the social conditions of the patients were favourable which explains the satisfactory development of the healthy children. Since they were less than 3 years old, mental development could not be tested by the usual methods. Therefore, we used certain variants of the Bühler—Hetzer test such as playfulness, attention, kinetic development, perception of colours and shapes, as also the children's ability of orientation on their own body. Information about emotional development and behaviour was provided by the parents.

We were surprised to find that the major half of the children passed the

TABLE IV

Distribution of the children according to duration of pregnancy and birth weight

Weight (g)	Pregnancy, weeks				Total
	28—32	33—34	35—37	38—42	
1501—2000	2		1		3
2001—2500		2	1	1	4
2501—3000			3	30	33
3001—4500			3	128	131
Total	2	2	8	159	171

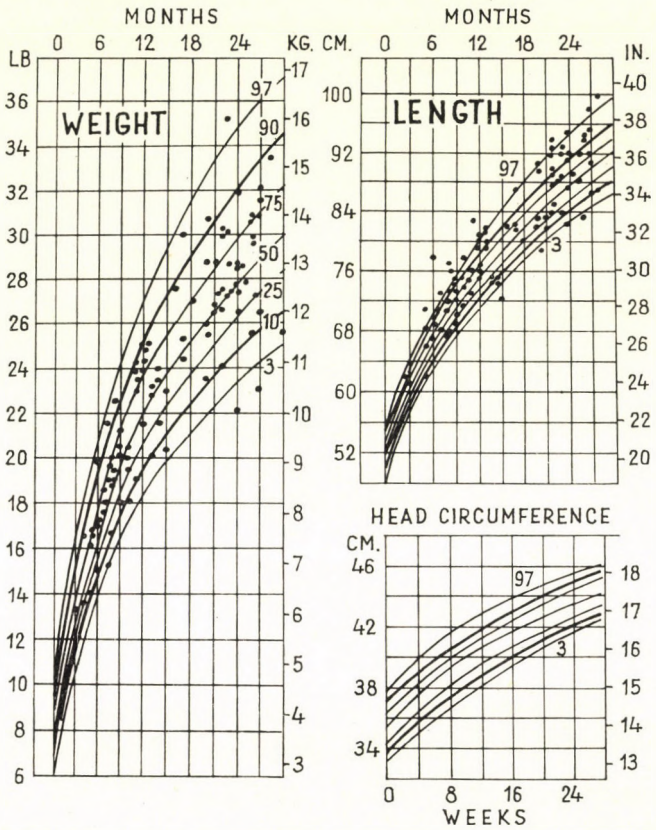

FIG. 1. Distribution of male children according to weight, body length and head circumference

tests considerably better than the average of their respective age groups. There was a single exception, a 2-year old child, whose slight mental retardation must have been due to repeated respiratory diseases and otitis. No disturbance of emotional development was observed. It should be noted that the psycho-social conditions of the patients were favourable and for a few exceptions, children under 18 months had been kept in the family.

At the physical examinations even the slightest signs of congenital malformation were carefully looked for. We found two such cases, a ventricular septum defect and an aortic stenosis. One of the mothers had been examined in the 24th, the other in the 43rd week (each in a single instance), that is, long after that phase of pregnancy which is critical from the point of view of foetopathies. We found, in addition, coxal dysplasia in two, strabismus in six cases and inguinal hernia in one case. The observed incidence of congenital anomalies was, therefore, not significantly different from that of the general population of

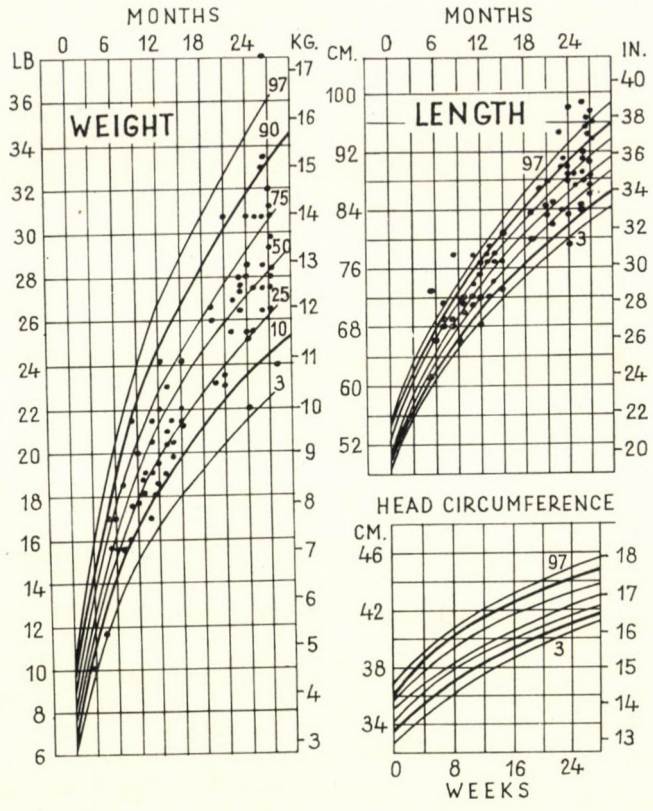

FIG. 2. Distribution of female children according to weight, body length and head circumference

Budapest. A 26-month old child had impaired hearing. This patient had been treated with streptomycin in two instances on account of repeated episodes of otitis.

Twenty randomly selected children were examined for chromosomal disorders; 10 had been exposed to ultrasound in utero and 10 normal controls. The karyogram of 1060 cells was evaluated in the test group and that of 980 cells in the control group. Results are shown in Table V, details in Tables VI and VII. Only two among the examined cells displayed a chromosomal aberration: one a dicentric chromosome, the other a reciprocal translocation. Comparison with the controls showed the difference to be non-significant statistically ($\chi^2 = 0.5341$; $p > 0.10$) so that all these are normal values [26].

Discussion

It is evident from the foregoing that physical and mental development of the examined children were like (and in some respects even better than) those of the general population,

TABLE V

Chromosomal examinations in children exposed

Ultrasound	Mean age, months	Number of cases	Number examined karyograms	Chromosome number					
				Hypo		Hyper		Poly	
				No.	%	No.	%	No.	%
Exposed	18.9	10	1060	33	3.3	3	0.3	1	0.1
Not exposed	16	10	980	26	2.6	2	0.2	1	0.1

TABLE VI

Chromosomal examination of children exposed to ultrasound

Serial number	Age (months)	Number of cells analysed	Number of ultrasound examinations	Number of hypomodal cells			Number modal cells	Number of hypermodal cells		Number of polyploid cells
				43	44	45		47	48	
1	32	100	2			1	98	1		
2	13	100	1			1	99			
3	24	100	2	2	3	1	94			
4	17	100	5		2	2	96			
5	17	100	5			3	96	1		
6	26	100	3		1	2	96		1	
7	12	100	1	1	2		96		1	
8	24	100	3		3	1	96			
9	13	100	1		4	2	94			
10	11	160	3		2	1	57			
Total	$\chi = 18.9$	1060	$\chi = 2.6$	3	17	14	922	2	1	1

nor did the incidence of congenital anomalies exceed the normal average. The number of the observed chromosomal aberrations, too, was in line with that of the general average. These results are in harmony with those of BOYD et al. [3] who likewise failed to reveal chromosomal damage after intrauterine ultrasound exposure. Re-examining MACINTOSH's earlier findings, COAKLEY et al. [4] discovered that the chromosomal damage must have been caused by the release of "toxins" from the polyethylene container in which ten cells were irradiated. In a recent paper, MACINTOSH [16a], too, has revised his earlier findings.

Thus, the results of earlier in vitro and animal experiments have now been confirmed by human clinical examinations. The present observa-

and not exposed to ultrasound

Disorders of chromatid type		Disorders of chromosome type							
		Labile						Stable	
No.	%	ace		dic		r		No.	%
		No.	%	No.	%	No.	%		
34	3.3	4	0.4	1	0.1			1	0.1
28	2.8	6	0.6						

TABLE VII

Incidence of chromosomal aberrations in children exposed to ultrasound in utero

No. of cases	Chromatid type			Chromosome type					
				Labile			Stable		
	Chromatid defect	Isochromatid defect	Chromatid breakage	ace	dic	r	t	inv.	dele
1*	4		1	1	1				
2	2			1					
3	1								
4*	2						1		
5	1	1							
6	2		1	1					
7	6		1						
8	4			1					
9	5								
10	2								
Total	29	1	3	4	1		1		

* = No new chromosome type aberration was observed in additional 100 cells

tions have further confirmed the opinion that diagnostic ultrasound exposure of pregnants is harmless for both the mother and her foetus.

REFERENCES

1. BESSLER, W.: Ultraschallwirkungen an Embrionen von Triton alpestris. Strahlentherapie **89,** 292 (1952).
2. BRETTSCHNEIDER, H.: Studien zur biologischen Wirkung des Ultraschalls auf die lebende Zelle. Strahlentherapie **87,** 517 (1950).
3. BOYD, E., ABDULLA, A., DONALD, I., FLEMING, J. E. E., HALL, A. I., FERGUSON-SMITH, M. A.: Chromosome breakage and ultrasound. Brit. med. J. **2,** 501 (1971).
4. COAKLEY, A., SLADE, J. S., LAURENCE, K. M.: Chromosome aberrations after exposure to ultrasound. Brit. med. J. **1,** 109 (1971).
5. CZEIZEL, E.: Terhesség alatti ultrahang vizsgálatok esetleges genetikai veszélyeiről. Orv. Hetil. **112,** 412 (1971).
6. DONALD, I., BROWN, T. G.: Demonstration of tissue interfaces within the body

by ultrasonic echo sounding. Brit. J. Radiol. **34,** 539 (1961).
7. Falus, M., Sobel, M.: Missed abortion diagnosisa ultrahanggal. Orv. Hetil. **110,** 2581 (1969).
8. Falus, M., Sobel, M.: A magzati szívműködés kimutatása ultrahanggal. Orv. Hetil. **111,** 2539 (1970).
9. Fischer, E.: Basic biological effect of ultrasonic energy. Amer. J. phys. Med. **33,** 174 (1954).
10. Fischer, P. E., Golob, A., Kratochwil, A.: Chromosomenuntersuchung nach Ultraschallwirkung. Wien. klin. Wschr. **79,** 436 (1967).
11. Fry, W. J., Fry, F. J.: In: E. Kelly: Ultrasound in Biology and Medicine. American Institute of Biological Sciences Washington, D. C. 1957.
12. Howry, D. M.: In: E. Kelly: Ultrasound in Biology and Medicine. American Institute of Biological Sciences, Washington, D. C. 1957.
13. Kratochwill, A.: Ultraschalldiagnostik in Geburtshilfe und Gynäcologie. Georg Thieme, Stuttgart 1968.
14. Kamocsay, D.: Ultrasound in Gynecology. Amer. J. phys. Med. **37,** 196 (1958).
15. Khentow, R. A.: Data Concerning the Use of Ultrasound for Diagnosis in Medicine. Inst. med. Instr. **3,** 109 (1966)
16. MacIntosh, I. J. C., Davey, D. A.: Chromosome aberrations induced by an ultrasonic fetal pulse detector. Brit. med. J. **4,** 92 (1970).
16a. MacIntosh, I. J. C.: Chromosome breakage and ultrasound. Brit. med. J. **3,** 703 (1971).
17. Mosler, K. M.: Chromosomenschäden durch Ultraschall in der geburtshilflichen Diagnostik. Med. Trib. **6,** 3 (1971).
18. Neubauer, Gy., Hernádi, G., Falus, M.: A placentographiáról. Orv. Hetil. **111,** 1203 (1970).
19. Rott, O.: Schädigung des Feten bei Ultraschallüberwachung während Risikogravidität wirklich auszuschliessen? Med. Trib. **6,** 617 (1971).
20. Serr, D. M., Padeh, B., Zakut, H., Shaki, R., Mannor, S. M., Kalner, B.: European Congress of Perinatal Medicine. S. Karger, Basel 1970.
21. Sunden, B.: On the diagnostic value of ultrasound in obstetrics and gynecology. Acta obstet. gynec. scand. **1,** (Suppl. 6) 43 (1964).
22. Sobel, M., Falus, M.: A magzat korának meghatározása ultrahanggal. Orv. Hetil. **111,** 2595 (1970).
23. Wild, J. J.: The use of ultrasonic pulses for the measurement of biologic tissues and the detection of tissue density changes. Surgery **27,** 183 (1950).
24. Wild, J. J.: The effect of biological tissues on the histologic structure of tumors of the living intact human breast. Amer. J. Path. **28,** 839 (1952).
25. Woeber, K. M., Veltmann, G.: Ultraschall in der Medizin. Steinkopff, Dresden 1963.
26. Court Brown, W. H.: Human Population Cytogenesis. North-Holland Publ. Co., Amsterdam 1967.

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