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Birth prevalence of five congenital abnormalities of medium frequency in Budapest

by

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In Budapest, 1970—1977, the birth prevalence of isolated renal agenesis, exomphalos-omphalocele, anal atresia, tracheo-oesophageal fistula with oesophageal atresia or stenosis, and diaphragmatic hernia was 0.23, 0.20, 0.18. 0.18 and 0.16,respectively, per 1000 total births. The birth prevalences of multiple abnormalities which were sharply distinguished from the isolated cases were in the order of the above-mentioned abnormalities 0.13, 0.19, 0.18, 0.14 and 0.19, respectively, per 1000 total births. The last ones are partly associations (e.g. Vacterl) and partly random combinations. The rates of the capital Budapest might be representative for the birth prevalences of these congenital abnormalities in Hungary in the 1970's.

Congenital abnormalities (CAs) which have become one of the 10 main causes of death can be classified according to their birth (live and stillbirth) prevalence. Thus, three categories of CAs can be separated, *viz.* (i) common CAs with a birth prevalence of more than 1 per 1000 total births; (ii) medium frequent CAs with a birth prevalence between 1 and 0.1 per 1000 total births; and (iii) rare CAs whose birth prevalence is less than 0.1 per 1000 total births. In Hungary, 65% of the cases are common CAs (Table I). Out of these, the aetiology of nine isolated common CAs can be described by the multifactorial threshold model, while the 10th condition, Down syndrome, can be traced back to the trisomy of chromosome 21. Another 20% is caused by further 20 CAs of medium frequency. The remaining 15% consists of more than 1000 rare CAs. Up to now the birth prevalence of 15 medium frequent CAs has been known

Table I

Birth prevalences of common congenital abnormalities in Hungary

Common congenital abnormality	Birth prevalence per 1000 total births
Anencephaly — spina bifida cystica	2.90±0.38
Cleft lip±palate	1.06±0.10
Congenital hypertrophic pyloric stenosis	1.51±0.12
Ventricular septal defect	1.63±0.22
Congenital dislocation of the hip	27.77±0.50
Congenital structural talipes equinovarus	1.52±0.25
Congenital inguinal hernia	1.14±0.37
Hypospadias	4.44±0.61
Undescended testicles	13.53±1.24
Down disease	1.17±0.11

TABLE II

Birth prevalences of medium frequent congenital abnormalities (CA) in Hungary

Code number of ICD	CA	Birth prevalence per 1000 total births
742.0	Congenital hydrocephalus	0.76
743.0	Encephalocele	0.22
743.1	Microcephaly	0.20
746.0	Common truncus	0.27
746.1	Transposition of great vessels	0.31
746.4	Atrial septal defect	0.91
747.0	Patent ductus arteriosus	0.86
747.1	Coarctation of aorta	0.40
747.2	Aortic stenosis	0.57
747.3	Pulmonary stenosis	0.29
749.0	Cleft palate	0.42
753.1	Cystic kidney disease	0.14
755.0	Polydactyly	0.30
755.1	Syndactyly	0.25
755.2	Reduction deformities of limbs	0.41

in Hungary (Table II). In this paper the birth prevalence of further five medium frequent CAs, namely of *a*nal *a*tresia (AA), *t*racheo-*o*esophageal *f*istula with oesophageal atresia or stenosis (TEF), *r*enal *a*genesis (RA), *h*ernia *dia*phragmatica (HeDia) and *exo*mphalos-omphalocele (Exo) will be published for the total births of Budapest between 1970 and 1977.

The epidemiological survey has been based on the assumption that index patients with these types of CAs either die or are operated upon. There being no third possibility, they could be found without exception in the records of the institutes of pathology and paediatric surgery. Our purpose, on the one hand, was to determine the birth prevalences, i.e. the so-called p-values of the above-mentioned five medium frequent CAs and on the other hand to check the completeness of their registration in the Hungarian Congenital Malformation Register.

MATERIAL AND METHOD

The study population included the total births (220,088 live births and 1,921 stillbirths) of the inhabitants of Budapest from January, 1970, to December 31, 1977.

In the course of diagnoses, the following types were included or excluded.

AA can be the consequence of at least four different developmental processes [8], thus it would be advisable to make a distinction between Type 1: anal stenosis; Type 2: membranous imperforate or covered anus; Type 3: anorectal atresia (imperforate anus with a rectal pouch ending some distance above the anus); and Type 4: rectal atresia or stenosis. We were, however, unable to solve the separation of these types of AA.

Gross [8] distinguished five types of TEF. Type C, i.e. the upper oesophageal segments ending in blind pouch and the lower segment communicating with the trachea, has the highest occurrence.

RA did, of course, not include polycystic kidneys, congenital renal dysplasia and other CAs of the kidney which often lead to a clinically similar disease (Potter anomalad).

In the case of HeDia it was not always possible to separate true HeDia from pseudo-hernias, neither could the separation of total and partial HeDias be solved.

A sharp distinction has to be made between Exo and (i) gastroschisis (para-

omphalocele), but the differential diagnosis of these two CAs was not solved at the time of the study, and (ii) minor anomalies requiring no surgical treatment, such as umbilical hernia; furthermore (iii) the agenesis of the abdominal musculature; (iv) insufficient closure of the musculature of the anterior abdominal wall (e.g. exstrophy of bladder or cloaca); and (v) the abdominal muscle deficiency (prune belly syndrome) anomalad [7, 13].

Isolated and multiple CAs (5) were separated from each other. A primary CA associated with a secondary CA was considered an anomalad [1] classified as an isolated CA.

The ascertainment of index patients involved the processing of the necropsy records in 21 pathological institutes of Budapest and of the surgical records of 7 departments of paediatric surgery. The following data of the records were noted: name and address of the parents and time and place of birth of index patients, type of birth (live or stillbirth), birthweight and week of gestation, birth order (if given), fate of index patient (died or alive) and, finally, the diagnosis of CAs. By using an individual card for each child any multiple evaluation could be avoided.

Some cases of the five CAs studied could be lost partly if the stillborn was not subjected to necropsy or if it was not sufficiently thorough. With the exception of Exo this possibility had to be taken into consideration, but the likelihood of this error is not significant, since the participation of stillbirths was low in the study population. Partly, when the child of parents domiciled in Budapest was born or operated upon elsewhere and this was not entered into the records. These, however, are probably exceptional cases.

Finally, we selected the registered data of index patients with AA, TEF, RA, HeDia and Exo from the material of the Hungarian Congenital Malformation Register, 1970–1977, and compared these to the data of our epidemiological survey.

Results and Discussion

There is a considerable difference in aetiology between isolated and multiple CAs. Isolated CAs are presumably the manifestations of the same nosological unit, while the CAs within multiple CAs can be a symptom of a number of syndromes and associations of different origin. Clinical aspects, too, support the need of their separation: multiple CAs are far more severe and the presence of other CAs have a significant influence, for example on the outcome of the operation. Consequently, it is necessary to separate these two categories of CAs both from the nosological and the clinical point of view.

Among the isolated CAs (Table III), RA has the highest birth prevalence: 0.225 per 1000 total births (Table III). Of the 50 evaluated cases only 18 (36%) were single CAs, the other 64% involved anomalads (Potter and caudal regression: 28; abdominal muscle deficiency: 4). Bilateral renal agenesis nearly always becomes an anomalad. Only three of the 18 single cases were bilateral, although in these cases one of the kidney remnants, though severely hypoplastic, was still detectable. The other cases were unilateral. It is a matter of contention whether the classification of the four abdominal muscle deficiencies into this category is correct, since the latter can be considered an independent nosological unit. Without these four index patients with abdominal muscle deficiency the birth prevalence of isolated RA is 0.21 per 1000 total births.

The second most frequent CA within the group is Exo with a birth prevalence of 0.20 per 1000 total births. In 1975 far more Exo-s occurred than usual.

The birth prevalences of isolated AA and TEF were the same: 0.18 per 1000 total births. Surprisingly there was no TEF in 1971.

Isolated HeDia with a birth pre-

TABLE III

Number and birth prevalence of five isolated congenital abnormalities (CAs) in Budapest, 1970—1977. In brackets, the number of cases with gastroschisis is shown

CA / Year	AA	TEF	RA	HeDia	Exo
1970	3	7	3	1	4 (—)
1971	7	—	4	5	3 (1)
1972	2	8	9	2	6 (1)
1973	4	2	10	2	4 (—)
1974	5	5	5	5	6 (1)
1975	8	5	4	6	13 (2)
1976	8	4	8	5	6 (1)
1977	4	8	7	9	2 (2)
Number	41	39	50	35	44 (8)
Total per thousand	0.18	0.18	0.23	0.16	0.20

TABLE IV

Data of the studied congenital

CA	Isolated (Single)		Multiple: with other CAs		Together	
	No.	Per thousand	No.	Per thousand	No.	Per thousand
AA	41	0.18	41	0.18	82	0.37
TEF	39	0.18	30	0.14	69	0.31
RA	50	0.23	29*	0.13	79	0.36
HeDia	35	0.16	43	0.19	78	0.35
Exo	44	0.20	42	0.19	86	0.39
Total	209	0.94	185	0.83	394	1.77

* 1 case each of Down syndrome and holocardius amorphus.

TABLE V

Number of associated congenital abnormalities (CAs) within multiple cases

CA \ Number of combinations	2	3	4	5	6	7	8	Total
AA	22	6	5	5	1	2	—	41
TEF	11	10	4	4	—	—	1	30
RA	17	4	4	4	—	—	—	29
HeDia	24	12	5	1	1	—	—	43
Exo	20	11	5	5	—	1	—	42
Total	94	43	23	19	2	3	1	185

valence of 0.16 per 1000 total births is presumably the sum of several different nosologic units.

Evaluation of the CAs studied appearing as part of multiple CAs is shown in Tables IV and V, as well as in Fig. 1.

Before assessing the cases of multiple RA, three preliminary remarks have to be made. (i) The Potter and caudal regression anomalads were not considered separately as they are secondary consequences of bilateral RA. In the cases of multiple RA almost always the anomalads were observed. (ii) The participation of congenital cardiovascular malformations is presumably exaggerated. In six cases only "congenital heart defect" and in four patent ductus arteriosus were mentioned. The former is an unreliable, doubtful diagnosis, the latter is not an absolute indication of CA in infants died

abnormalities (CAs)

Notification				No notification		Misdiagnosis (excluded)	
correct		incorrect					
No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
52	63.4	20	24.4	10	12.2	2	2.4
45	65.2	11	15.9	13	18.9	3	4.3
25	31.6	21	26.6	33	41.8	2	2.5
40	51.3	16	20.5	22	28.2	3	3.8
52	60.5	20	23.2	14	16.3	4	4.7
214	54.3	88	22.3	92	23.4	14	3.6

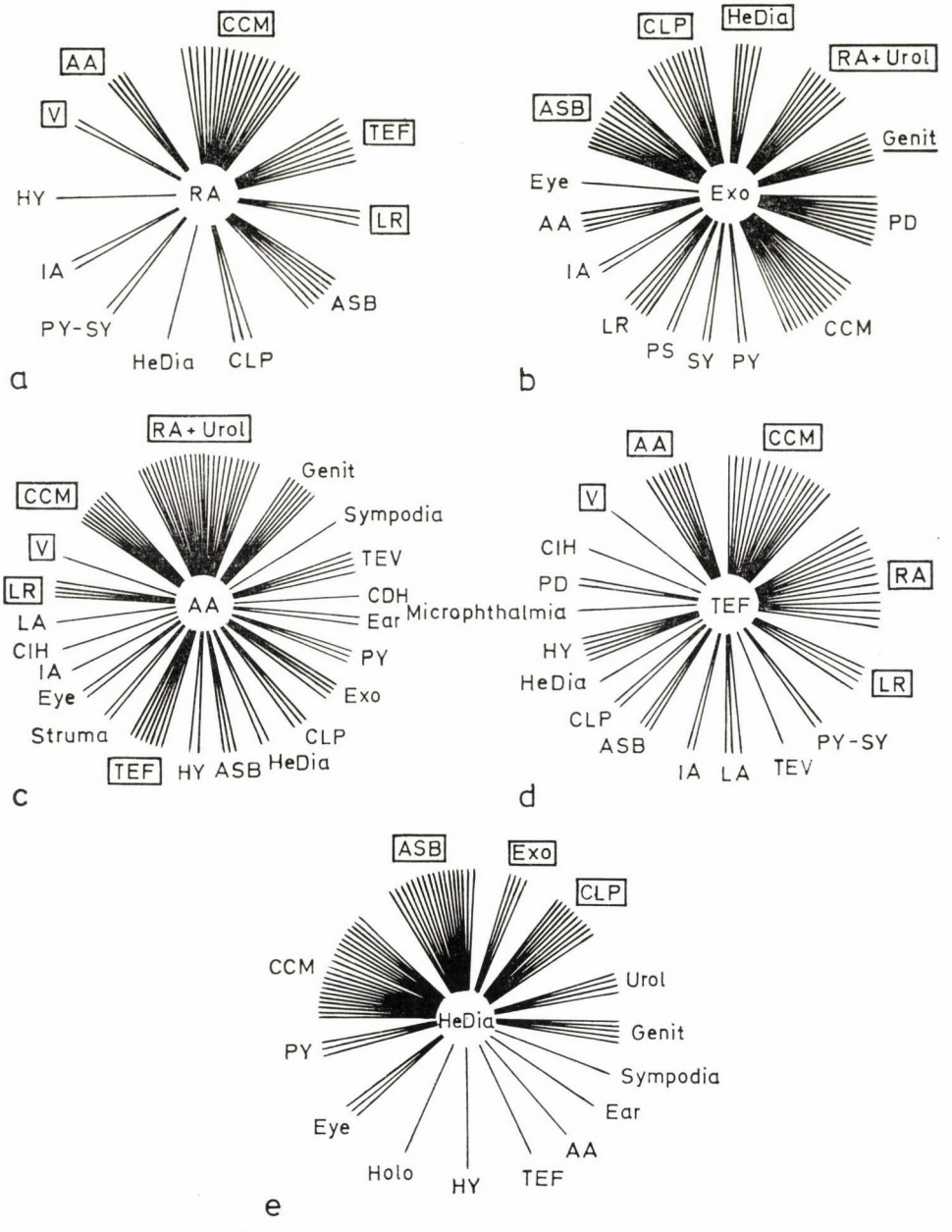

FIG. 1. Distribution of congenital abnormalities within multiple RA(a), Exo(b), AA(c) TEF(d) and HeDia(e)

CCM	= congenital cardiovascular malformation	HY	= hydrocephalus
TEV	= talipes equinovarus	V	= vertebral anomalies
LR	= limb reduction	Urol	= urological anomalies
ASB	= anencephaly–spina bifida cystica	Genit	= genital anomalies
CLP	= cleft lip ± palate	PD	= postural deformities
PY	= polydactyly	PS	= pyloric stenosis
SY	= syndactyly	CDH	= congenital dislocation of the hip
IA	= intestinal atresia	CIH	= congenital inguinal hernia
		LA	= laryngeal atresia
		Holo	= holoprosencephaly

perinatally. (iii) There were two cases of specified syndromes: Down and holo-acardius amorphus. Consequently, the birth prevalence of 0.13 per 1000 total births of multiple RAs seems too high. The combinations of two CAs dominate but the majority of them might be isolated RA because of the unreliable diagnosis of congenital cardiovascular malformations. The number of three, four and five associated CAs is the same. The outlines of the VACTERL-association are obvious: RA is often associated with vertebral CA, AA, cardiac CA, TEF and radial limb defects (these are specially marked in Fig. 1/a). It is questionable whether the frequent association between RAs and neural tube defects indicates an inclination to vertebral association or is an independent combination. Three oral clefts are also worth mentioning. The other CAs can be the consequence of random combinations.

The birth prevalence of 0.19 per 1000 total births of index patients with multiple Exo was practically the same as that of isolated Exo. The combination of two CAs dominates which is somewhat suspicious, as syndromes and true associations consist only seldom of not more than two CAs. Here, too, eventual secondary consequences and the unreliable diagnosis of congenital cardiovascular malformations have to be considered. In the case of multiple Exo-s the outlines of the ADAM and schisis-association [6] is quite conspicuous (Fig. 1/b). Typical anomalads of RAs occur more often than permitted by random combinations (caudal regression anomalad can have Exo too). The other associated CAs can be ascribed to random combinations.

Multiple AA has a slightly higher birth prevalence than multiple TEF. In the case of TEF the occurrence of the combinations of two and three CAs is almost the same. In the case of multiple combinations, the VACTERL-association may be outlined. The high occurrence of Exo should also be mentioned, the other CAs are probably random combinations.

Finally, we have to discuss the high birth prevalence (0.19 per 1000 total births) of HeDia. In these cases the high number of associations with congenital cardiovascular malformations calls for special caution. HeDia is an anomalad regularly associated with secondary dextrocardia or hypoplasia of the left heart. The congenital cardiovascular malformations shown in Fig. 1/e are not of these types, but four of them were only mentioned as "congenital heart defect" and four were patent ductus arteriosus. Thus a considerable part of the combinations of two CAs can be an artefact. The combinations of HeDia clearly show the existence of schisis-association. The others can be explained with random combinations.

Summing up, a more thorough ascertainment and evaluation of the isolated and multiple manifestations of CAs studied would lead to a rise in the birth prevalence of isolated CAs at the cost of multiple CAs.

It is not easy to compare the birth prevalence of the CAs studied in Budapest, 1970–1977, to the similar data of other countries. On the one hand, most studies have failed in making sharp difference between isolated and multiple CAs, while, on the other hand, the study population and samples are often different and the definition of CAs studied is not always given accurately. The overall birth prevalence of RA was between

TABLE VI

Birth prevalence of anal atresia (AA), tracheo-oesophageal fistula (TEF), hernia diaphragmatica (HeDia) and exomphalos-omphalocele (Exo) in countries and towns taking part in the WHO collaborative study

Sample	AA	TEF	HeDia	Exo
I. Melbourne I	—	0.38	0.03	0.38
Melbourne II	0.26	—	—	—
II. São Paolo	0.21	0.49	0.02	0.14
III. Santiago	0.04	0.04	—	0.08
IV. Bogota	0.27	—	—	0.05
Medellin	0.05	—	—	0.10
V. Czechoslovakia	0.20	0.20	0.40	0.05
VI. Alexandria	0.10	0.10	—	0.21
VII. Hong Kong	0.10	—	—	0.20
VIII. Bombay	0.30	0.08	0.03	0.20
Calcutta	0.10	—	—	0.05
IX. Kuala Lumpur	0.56	0.06	0.06	0.15
Singapore	0.15	—	0.08	0.07
X. Mexico City I	0.20	0.36	0.16	0.04
Mexico City II	0.28	—	0.14	—
XI. Belfast	0.14	0.21	0.04	0.11
XII. Panama City	0.13	—	0.25	—
XIII. Manila	0.07	0.03	0.13	0.07
XIV. Cape Town	—	—	—	0.33
Johannesburg	0.09	0.27	0.72	0.18
Pretoria	0.20	0.10	—	—
XV. Madrid	0.15	0.15	0.25	0.51
XVI. Ljubljana	0.11	0.11	0.23	—
Zagreb	0.24	0.12	—	0.24
Total	0.17	0.11	0.10	0.10
Budapest	0.18	0.18	0.16	0.20

TABLE VII

Number and birth prevalence of the studied congenital abnormalities notified from the country and Budapest in the material of the Hungarian Congenital Malformations Register, 1970–1976

Types of CA	Total material		Country material		Budapest material		Ascertained cases in Budapest with in special epidemiological study	
	No	Per thousand	No	per thousand	No	per thousand	No	per thousand
AA	210	0.18	176	0.18	34	0.18	37	0.19
TEF	199	0.17	175	0.18	24	0.13	31	0.16
RA	144	0.12	119	0.12	25	0.13	43	0.22
HeDia	227	0.19	206	0.21	21	0.11	26	0.14
Exo	217	0.18	180	0.18	37	0.19	42	0.22

0.3 and 0.4 [14, 9, 10], the birth prevalence of Exo between 0.1 and 0.3 [11, 15, 4], the birth prevalences of AA and TEF in general between 0.1 and 0.3 per 1000 total births [2, 3, 12, 17, 19]. The birth prevalence of HeDia was very different, varying from 0.05 to 0.2 per 1000 total births [18].

A comparison with the data of the WHO collaborative study involving 24 samples from 16 countries seems to be useful [16]. In this study, birth prevalences were based on the total births and the isolated and multiple cases were separated. Table VI shows the birth prevalences of four studied CAs: AA, TEF, Exo and HeDia in the WHO study, which did not include the birth prevalence of RA. The occurrence of isolated cases is as a rule, higher in Budapest than the average values in the WHO study; in the case of Exo the Hungarian values are twice as high as those in the WHO study. The birth prevalence of AA is almost the same. We believe that this might be due not so much to a higher objective birth prevalence in Hungary, but to a more complete ascertainment of index patients.

Finally, the data of the epidemiological survey of Budapest were compared to the corresponding data of the Hungarian Congenital Malformation Register (Table VII). Checking of the registered data for Budapest has shown that 12.2 to 41.8% of these CAs have not been notified. The completeness of notification is expressed by the complementary values, which was good in the cases of AA, TEF and Exo, and just sufficient in the cases of RA and HeDia. 15.9 to 26.6% of the cases were notified inaccurately which means first of all that notification of the associated CAs is lacking. In 2.4 to 4.7% of the cases the notified diagnosis was false; the complementary values for the latter indicate the validity of the registered diagnosis of CAs studied.

The birth prevalences of these CAs of medium frequency, with the exception of HeDia, show no significant

difference between Budapest and the country (Table VII). The inhabitants of Budapest amount to 20% of the Hungarian population. According to our experience, there is no significant difference in birth prevalence between the various types of CAs in Budapest and in the country, so that the birth prevalences of RA, Exo, AA and TEF in Budapest can be considered to be representative for the Hungarian population.

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