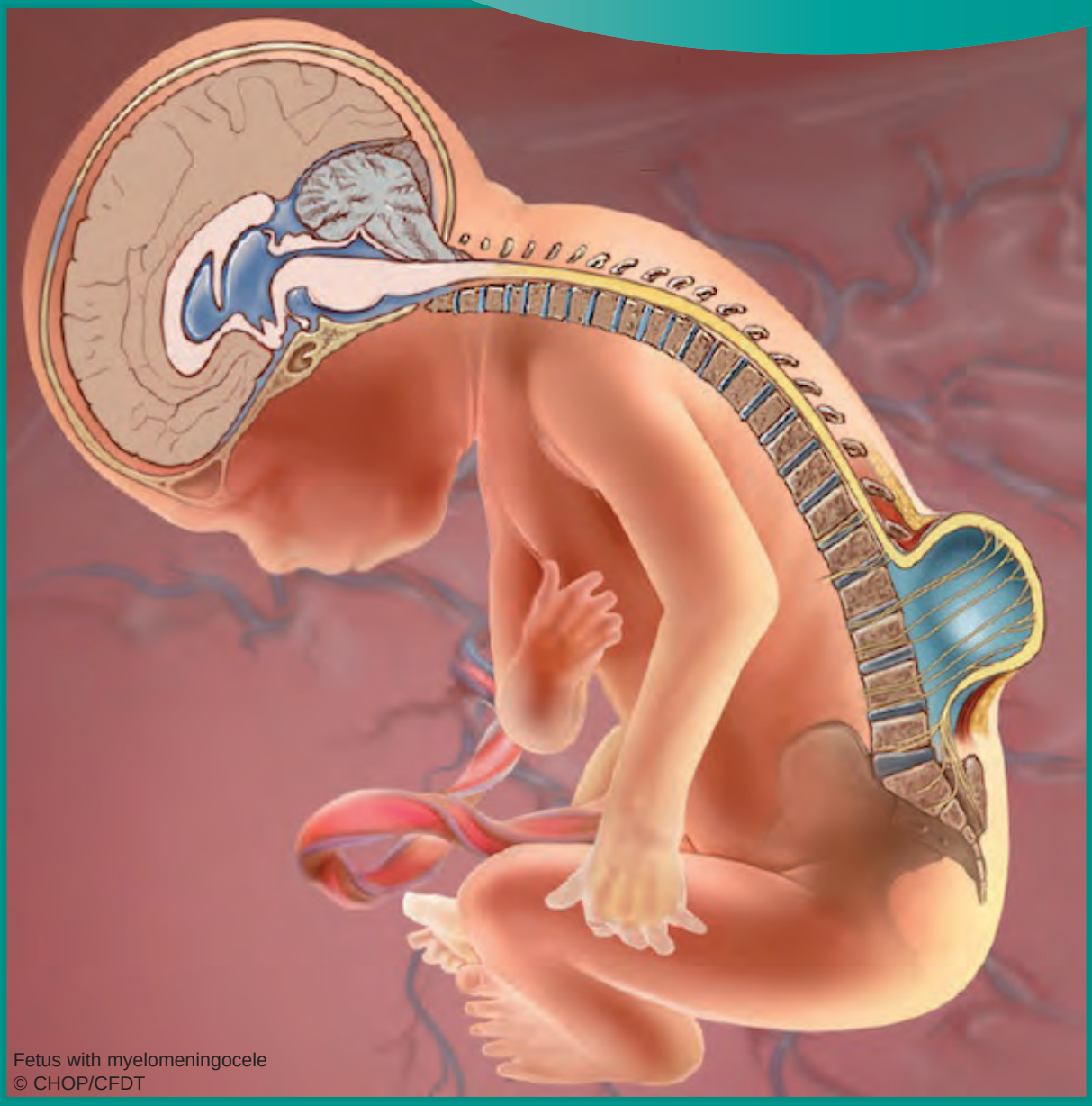
Annual Report 2011



Fetus with myelomeningocele
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Malformation Monitoring Centre Saxony-Anhalt

Medical Faculty

Otto-von-Guericke-University Magdeburg

SACHSEN-ANHALT
Ministerium für
Arbeit und Soziales

Annual Report 2011
of the Federal State of Saxony-Anhalt
about the frequency of congenital malformations
and anomalies as well as genetically caused diseases

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Introduction

Dear reader,

Having a child is wonderful and parents often hunger for the birth of their baby which needs all their love and care. The most important thing is that a child is born healthy, however, unfortunately, this wish does not always become true. The employees of the Malformation Monitoring Centre Saxony-Anhalt know this very well.
During the period of pregnancy parents often have many questions and since diverse medical care is offered they take every opportunity to protect mother and child. In this connection the preventative health care plays one of the most important roles and the Malformation Monitoring Centre Saxony-Anhalt forms part of the preventative health care system. When parents have confidence in the medical care and over all have trust in their attending physician a firm basis is created to care for the child at an early stage, to provide help and from view of the parents to accept this help. Health promotion and prevention, e.g. special dietary advice are important tasks during this period of time.
The development of a child is a complex process and during the first years of life the steps in its development are huge. All the more it is reassuring to know that the examinations during pregnancy regularly check the general health condition and the age-appropriate development of the baby. By this way problems or abnormalities can be detected at an early stage and the adequate treatment can be supplied. Parents are informed as well about further examinations within the early detection program which might support a healthy development of a child.

The present Annual Report 2011 of the Malformation Monitoring Centre Saxony-Anhalt outlines as "special topic" in this year neural tube defects. These embryonic defects may appear during pregnancy which means that a disorder occurs when the central nervous system is formed. Consequently, the embryonic development is sorely afflicted and the child later often physically handicapped. Different types of the neural tube defects exist and they are also called "spina bifida". Approximately one per cent of the German population suffers from a neural tube defect, whereby the degree of severity of the malformation may differ very much.

The Malformation Monitoring Centre Saxony-Anhalt collects and analyses relevant data since 1980 with the purpose to create a basis for the evaluation of trends and clusters in the appearance of congenital malformations and anomalies. By registering these essential epidemiological information possible risk factors for the occurrence of congenital malformations might be detected and the efficiency of primary prevention can also be reviewed when analysing the collected data.
In 1992 the Malformation Monitoring Centre Saxony-Anhalt became a member of EUROCAT (European Surveillance of Congenital Anomalies) which is a European Association of 43 malformation monitoring centres from 23 countries. These departments monitor together one third of the European birth population with regard to congenital malformations. The consolidation of data from the single departments serves to analyse trends of a considerably bigger population. Even a sufficient number of only rare appearing malformations might be accepted for statistical evaluations in this way. Furthermore, the Malformation Monitoring Centre Saxony-Anhalt represents Germany with its data at the ICBDSR (International Clearinghouse for Birth Defects Surveillance and Research), an International Association of malformation registries.

At the end, please allow me to take the opportunity and thank all participants at the maternity clinics for the detailed and anonymised data transmission to the Monitoring of Congenital Malformations. Especially, I wish to thank Dr. med. Anke Rißmann and her team for their solid and high quality work when compiling this Annual Report 2011.

Norbert Bischoff
Federal Minister of Labour and Social Affairs Saxony-Anhalt

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Abbreviations

AABR	automated auditory brainstem response
ASD	atrial septal defect
bil.	bilateral
BMI	Body-Mass-Index
BP	basic prevalence
BPA	British Pediatric Association
CI	Confidence Interval
CNS	central nervous system
dB	decibel
DD	differential diagnosis
DIV	double inlet ventricle
DORV	double outlet right ventricle
EUROCAT	European Surveillance of Congenital Anomalies
ENT	ears, nose and throat
G-BA	Federal Joint Committee (Gemeinsamer Bundesausschuss)
ICBDSR	International Clearinghouse for Birth Defects Surveillance and Research
ICSI	intracytoplasmatic Sperm injection
LB	live births
MCA	multiple congenitale anomalies
n. o. s.	not otherwise specified
n. s..	not specified
NT	nuchal translucency
P	prevalence
PDA	persistend ductus arteriosus
PFO	persistend foramen ovale
SA	spontaneous abortion
SB	stillbirths
s. o.	suspicion of
TEOAE	transitory evoked otoacoustic emissions
TOP	termination of pregnancy
VSD	ventricular septal defect
WOG	weeks of gestation

1 Saxony-Anhalt - Registration Area

2 Birth Rate 2011

	Live births*	Stillbirths*	Spontaneous Abortions (> 16 WOG)	Terminations of Pregnancy	Total
Altmarkkreis Salzwedel	660	-	-	1	**661**
Anhalt-Bitterfeld	1,167	3	-	1	**1,171**
Börde	1,333	5	1	6	**1,345**
Burgenlandkreis	1,231	7	-	1	**1,239**
Dessau-Roßlau	575	-	-	3	**578**
Halle	2,106	12	1	8	**2,127**
Harz	1,513	7	-	6	**1,526**
Jerichower Land	624	2	3	2	**631**
Magdeburg	2,043	9	13	13	**2,078**
Mansfeld-Südharz	943	6	1	4	**954**
Saalekreis	1,423	7	1	6	**1,437**
Salzlandkreis	1,388	4	5	3	**1,400**
Stendal	907	4	-	2	**913**
Wittenberg	924	3	-	2	**929**
Major cities: Dessau-Roßlau, Halle, Magdeburg	4,724	21	14	24	**4,783**
Districts, in total	12,113	48	11	34	**12,206**
Saxony-Anhalt	**16,837**	**69**	**25**	**58**	**16,989**

* Federal Statistical Office Saxony-Anhalt 2012

3 Participating Institutions of the Region 2011

3.1 Materny units / paediatric units (ordered by location)

- AMEOS Klinikum Aschersleben
- AMEOS Klinikum Bernburg
- Gesundheitszentrum Bitterfeld/Wolfen gGmbH
- Krankenhaus Jerichower Land GmbH Burg
- Städtisches Klinikum Dessau
- Altmark-Klinikum gGmbH Krankenhaus Gardelegen
- AMEOS Klinikum St. Salvator Halberstadt
- Sana Ohre-Klinikum GmbH Haldensleben
- Krankenhaus St. Elisabeth und St. Barbara Halle
- Universitätsklinikum Halle (Saale)
- Krankenhaus Köthen GmbH
- Klinik St. Marienstift Magdeburg
- Klinikum Magdeburg gGmbH
- Universitätsklinikum Magdeburg A.ö.R.
- Carl-von-Basedow-Klinikum Saalekreis GmbH Merseburg
- Saale-Unstrut Klinikum Naumburg
- Bördekrankenhaus GmbH Neindorf
- Harzklinikum Dorothea Christiane Erxleben GmbH Quedlinburg
- Altmark-Klinikum gGmbH Krankenhaus Salzwedel
- HELIOS Klinik Sangerhausen
- AMEOS Klinikum Schönebeck
- Johanniter-Krankenhaus Genthin-Stendal gGmbH
- Asklepios Klinik Weißenfels
- Harz-Klinikum Wernigerode-Blankenburg GmbH
- Georgius-Agricola Klinikum Zeitz
- Krankenhaus Zerbst GmbH
- *Herzzentrum Leipzig, Klinik für Kinderkardiologie (außerhalb von Sachsen-Anhalt)*

3.2 Institutions of pre- and postnatal diagnostics (ordered by location)

- Dipl.-Med. Heweker, Fachärztin für Frauenheilkunde und Geburtshilfe, Bernburg
- Frau Grimm, Glindenberg/Magdeburg
- AMEOS Klinikum St. Salvator Halberstadt, Pränatale Ultraschalldiagnostik: CA Dr. Schmidt
- Dres. Perlitz, Fachärzte für Frauenheilkunde und Geburtshilfe, Haldensleben
- PD Dr. Hahmann, Facharzt für Frauenheilkunde und Geburtshilfe, Halle
- Krankenhaus St. Elisabeth und St. Barbara Halle, Pränatale Ultraschalldiagnostik: CA Dr. Seeger / OA Dr. Seliger
- Universitätsklinikum Halle (Saale), Pränatale Ultraschalldiagnostik:
  CA Prof. Dr. Tchirikov / OA Dr. Thäle / OÄ Dr. Scheler
- Dr. Altus, Fachärztin für Humangenetik, Magdeburg
- Dr. Karstedt, Facharzt für Kinder- und Jugendmedizin, Kinderkardiologie, Magdeburg
- Dr. Karsten, Facharzt für Frauenheilkunde und Geburtshilfe, Magdeburg
- Universitätsklinkum Magdeburg A.ö.R., Institut für Humangenetik
- Universitätsklinkum Magdeburg A.ö.R., Universitätsfrauenklinik, Pränatale Ultraschalldiagnostik: OÄ Dr. Gerloff
- Universitätsklinkum Magdeburg A.ö.R., Universitätskinderklinik, Screeninglabor
- Universitätsklinkum Magdeburg A.ö.R., Universitätsklinik für Orthopädie
- Trackingstelle Neugeborenenhörscreening Sachsen-Anhalt, Magdeburg
- Dipl.-Med. Fiedler und Giesecke, Fachärzte für Orthopädie, Merseburg
- Dr. Schneider, Facharzt für Frauenheilkunde und Geburtshilfe, Naumburg
- Altmark-Klinikum gGmbH Krankenhaus Salzwedel, Pränatale Ultraschalldiagnostik: CA Dr. Müller
- Dr. Woltersdorf, Fachärztin für Frauenheilkunde und Geburtshilfe, Schönebeck
- Johanniter-Krankenhaus Genthin-Stendal gGmbH, Pränatale Ultraschalldiagnostik: CA Dr. Henschen / CA Dr. Müller
- Harz-Klinikum Wernigerode-Blankenburg GmbH, Pränatale Ultraschalldiagnostik: OÄ Dr. Schulze

3.3 Pathological-anatomical instituts (ordered by location)

- AMEOS Klinikum Aschersleben, Abteilung Pathologie
- Institut für Pathologie Dr. Taege und Dr. Bilkenroth, Eisleben
- Universitätsklinikum Halle (Saale), Institut für Pathologie / Institut für Rechtsmedizin
- Klinikum Magdeburg gGmbH, Institut für Pathologie
- Universitätsklinikum Magdeburg A.ö.R., Institut für Pathologie
- Praxis für Pathologie, Dr. Lüders, PD Dr. Schultz und Dr. Braxein, Stendal

4 Malformation Registration in Saxony-Anhalt

4.1 General Information

The present Annual Annual Report 2012 outlines in the current year again substantial information regarding epidemiology of congenial malformations in Saxony-Anhalt. We have chosen as special topic in chapter 16 this time neural tube defects. Extensive scientific investigations regarding the prevalence of neural tube defects in a international context (in which we participated with data from Saxony-Anhalt) have the following result: The initial hope could not be fulfilled that by the means of folic acid prophylaxis the appearance of this complex malformation can be deleted completely.
The folic acid prophylaxis has limits in every day practice and therefore the neural tube defects still remain epidemiologically a challenging topic.

It is thanks to all our perinatologists (maternal-fetal medicine specialists and neonatolgists) in Saxony-Anhalt that we have such a low level of infant mortality in our Federal State. In comparison to other German Federal States Saxony-Anhalt ranges in the upper third since 2010. However, the reduction of infant mortality is directly connected with the topic of congenital malformations because they are the main reason for perinatal mortality in our Western world. Therefore, the ongoing data registration is an important requirement for a solid epidemiological analyses.

The Malformation Monitoring Centre Saxony-Anhalt started malformation registration in 1980 and is a member of EUROCAT (European Surveillance of Congenital Anomalies) since 1992. EUROCAT is the European Association of 43 malformation registration centres from 23 countries which monitor together 29% of the European population in regard to congenital malformations. The consolidation of data from the single departments serves to analyse trends of a considerably bigger population. Even a sufficient number of only rare appearing malformations might be accepted for statistical evaluations in this way. Furthermore, the Malformation Monitoring Centre Saxony-Anhalt represents Germany with its collected data at the ICBDSR (International Clearinghouse for Birth Defects Surveillance and Research), which is the International Association of malformation registers.

Saxony-Anhalt is the only Federal State in Germany with a region wide population-based malformation registration. This steady and high quality work is only possible due to the consistent support of the Ministry of Employment and Social Affairs of the Federal State of Saxony-Anhalt. At this point we would like to thank especially our persons in charge in the Ministry Dr. Dr. R. Nehring and Dr. H. Willer. We deeply regret the decease of Dr. H. Gunkel as we highly benefited from his support and many years of experience. Additionally, we would like to thank our colleagues Mrs. Dipl.-Wirtsch. V. Rätzel and Dr. J. L. Hülsemann at the Medical Faculty who constantly assist in organisational and administrative issues.
A special thanks goes to all our senders for their thorough and dedicated work since their collaboration is the most important factor for a successful work of the Monitoring of congenital malformations.

4.2 Registration and Analysis

The present report contains data about infants of the Federal State of Saxony-Anhalt with congenital malformations and chromosomal disorders in relation to the mother's place of residence during pregnancy, respectively at birth.

The total number of births includes:
- live births,
- stillbirths,
- terminations of pregnancy after prenatal diagnostics (all weeks of gestation)
- spontaneous abortions (>16 weeks of gestation)

and forms basis for the annual prevalence calculation.

The expected date of delivery is used as basis for analysing the termination of pregnancy, e.g. 2011 is considered the year of birth although induced termination of pregnancy took place at the end of 2010. This method is common on an international scale. In contrast, the time of delivery of spontaneous abortions is not corrected as the abortion is registered in the month when it actually took place.

The data of live births and stillbirths is provided anually by the Statistical Office of Halle.

All data transmitted to the Monitoring of Congenital Malformations is medically controlled upon receipt and the diagnoses are encoded according to ICD-10 and BPA. Details about the intake of medication during pregnancy are registered by using the internationally recommended ATC codes.

The present report outlines in chapter 7 and 8 the total number of infants with major malformations as well as the geographical distribution of appearance in the big cities and districts. Infants with only minor malformations or rather norm variations are not evaluated separately since this data is only collected incompletely in the end. The most frequent single diagnoses of major malformations registered in 2011 are outlined in Chapter 11.

Just as in the previous years the reported pathologic prenatal screening results are analysed separately in Chapter 10.

Chapter 12 contains again the analysis of the so-called indicator birth defects registered by the ICBDSR . As we have presented data in this way for a number of years, it is possible to evaluate the current prevalences of 2011 in comparison to the last 12 years (1999-2010). Here, a **total number of 205,635 births** forms basis for the **basic prevalence calculation 1999 to 2010**.
The graphical presentation of the annual prevalences allows to identify frequent appearances and gives an overview about rarely appearing indicator births defects. The exact calculation of confidence levels is based on the

binominal distribution with a confidence probability of 95%.

Our report outlines in chapter 13 data regarding geneticall-ly caused diseases, chromosomal disorders, sequences, associations, complexes and embryopathies. Chapter 14 contains an analysis of malformation caused terminations of pregnancy.

Chapter 16 is dedicated once more to a “special” topic and deals with neural tube defects in this year.

As in the previous years the Newborn hearing screening forms an inherent part of the Report of the Malformation Monitoring Centre Saxony-Anhalt and is outlined in chapter 18.

Chapter 19 presents the Annual Report of the department of newborn screening in Saxony-Anhalt with data regarding congenital metabolic disorders and endocrinopathies.

4.3 Data Quality and Completeness/Reporting Procedure

In 2011 the Malformation Monitoring Centre Saxony-Anhalt received information about 1,901 births. This number includes newborns and foetuses with congenital malformations as well as births without any malformation, which form a control group.

We have received 2119 data records for 2011. In 9.8% of all cases we received information from two or more institutions. By receiving these double-reportings it was often possible to classify complex malformations exactly or to reconfirm a diagnosis. In this way a steady high data quality can be assured.

The number of births and corresponding data records for 2010 increased after the publication of our last Annual Report from 2313 to 2341. The later registered births are now included into the analyses of the current report.

Unfortunately, the trend of completeness in regard to the gestational age (99.0%) and birth weight (97.4%) did not continue this year. However, a lot of important information was transmitted nearly completely thanks to the excellent work and effort of all senders. The relevant information was month of births (100%), gender (99.1%), maternal age (99.5%) and administrative district, respectively postal code (100%). More than two thirds of the missing birth weights were not registered in cases of terminations of pregnancy or spontaneous abortions. Missing gestational ages were not registered in case of some life births.

As in the previous years Chapter 10 of the present Annual Report analyses the prenatal ultrasound screening results we received from the participating gynaecologists. In this connection we are not able to state if a malformation that has been discovered during ultrasound screening was confirmed postnatal. Without confirmation of the finding or registration of the child/foetus by one of the participating institutions, we cannot include the diagnosis into our statistics. And it is probable that during the registration period 2011 in Saxony-Anhalt another anencephaly, holoprosencephaly, omphalocele, limb malformation or cystic kidney occurred. Therefore, we would like to ask again all obstetric clinics in Saxony-Anhalt to remember to complete a registration sheet when discovering a malformation.

The significance of the Annual Report mainly depends on complete and correct data records. We receive two thirds of malformation registrations and indications of control cases by means of the **"green documentation sheets"**, which we make available to the reporting institutions free of charge. Documentation sheets may be ordered at any time by phone **+49 391-6714174** or e-mail to **monz@med.ovgu.de**.

Additionally, it is also possible to report on so-called **"white documentation sheets"**. This form serves to register a minimum data set. The indication of the above mentioned information and possible risk factors like intake of medication or family history and an exact description of the malformation and corresponding symptoms are important here. It is not necessary that parents consent to the transmission of the malformation report by signing this form.

Mostly, we receive the reports by mail on our documentation form sheets. In many institutions fax reports have become the preferred method of transmission. Our fax number is: **+49 391-6714176**. Since the beginning of this year it is also possible to enter data **online** and send it via secure internet connection. Please contact us if you are interested in reporting your data online.

We will be at your disposal for answering any further questions about the reporting procedure and congenital malformations in general.

6 Sex Ratio

Sex ratio of all live births and stillbirths of Saxony-Anhalt according to the information of the Statistical Office Halle,

male	8,692 live births ans stillbirths
female	8,214 Lebend- und Totgeborene
total	16,906 Lebend- und Totgeborene

Sex ratio m : f = 1.06

The Statistical Office Halle registered in the year 2011 a total number of 16,906 life births and stillbirths which can be split up into 16,837 live births and 69 stillbirths. Compared to the previous year (17,363 life births and stillbirths) the total number of births in Saxony-Anhalt decreased about 3.0%.

The sex ratio of all live births and stillbirths shows with 1.06 again a light androtropism (2010: 1.04, 2009: 1.07). Similar to the previous years infants with major malformations show as well an androtropism with a value of 1.31 (2010: 1.23; 2009: 1.28).

Sex ratio of all births with major malformations (including abortions)

male	297 births
female	227 births
unknown	13 births
total	537 births

Sex ratio m : f = 1.31

Sex ratio of all births with only minor malformations and anomalies

male	132 births
female	119 births
total	251 births

Sex ratio m : f = 1.11

11 Organ System Involvement in Infants and Foetuses with Major Malformations

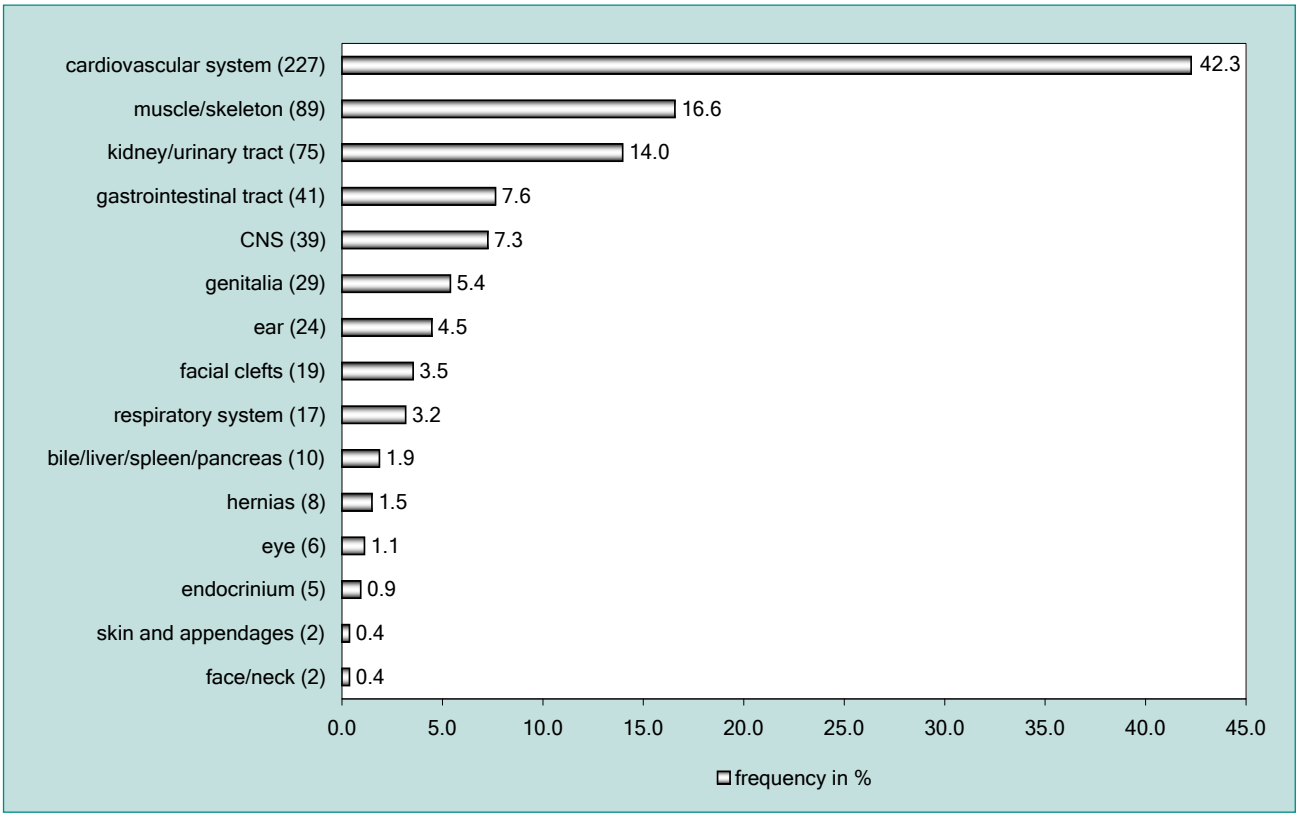


Fig. 5: Organ system involvement in major malformations (absolute figures and percentages of reported malformations)

Chapter 11 outlines the findings of all infants/foetuses with major malformations born in 2011. We registered 537 births with one or multiple major malformations whereby we classified the malformations according to organ system and registered in this way also infants/foetuses with several concerned organ systems. Births with chromosomal anomalies and MCA malformations without specification are not included in the figure.

227 births/foetuses with malformations of the cardiovascular system were registered in 2011. With a percentage of 42.3% malformations of this organ system form the biggest part among biths with major malformations. In comparison to 2010 (36.4 %, 215 births/foetuses) the value increased, however it is nearly similar to the value registered in 2009 (40.8 %).

The second place is occupied by malformations of the musculoskeletal system. The value decreased slightly compared to the previous year (2011: 16.6%; 2010: 19.3%). Major malformations of the kidney and urinary tract were registered in 2011 in 14.0% of the cases (2010: 16.4%). This time we registered more malformations of the gastrointestinal tract in infants/foetuses with major malformations than in the previous year (2011: 7.6%; 2010: 6.1%; 2009: 6.7%). While we registered 2010 a slightly increased number of CNS malformations (12.0%), the value in 2011 (7.3%) was even lower than in 2009 (9.9%). The malformation appearance of facial clefts (2011: 3.5%; 2010: 5.3%) and ears (2011: 4.5%; 2010: 5.4%) was also regressive in 2011.

As already mentioned some of our data records are postnatal incomplete so that the prenatal diagnosis could not be confirmed. This applies for a prenatally diagnosed omphalocele and limb malformation of an Edwards syndrome. All diagnoses that were not postnatally confirmed are not included in the analyses of chapter 12 of the present report.

In approximately four fifths of the prenatally found suspicious diagnoses we received information about the pregnancy outcome and the observed malformation. Since prenatal ultrasound screening forms an obligatory part of pre maternity care the transmission of prenatal and postnatal findings as well as information about pregnancy course and outcome are very important for the evaluation process. When comparing the results we can analyse their significance.

The most frequent single diagnoses 2011 (only major malformations)

	ICD 10	Diagnosis	Infants/Foetuses 2011		Infants/Foetuses 2000-2010 Prevalence /10.000
			Number	Prevalence /10.000	
1.	Q21.1	Atrial septal defect (inclusive persistent foramen ovale/PFO)	131	77.1	68.7
2.	Q21.0	Ventricular septal defect	59	34.7	44.6
3.	Q62.3	Other obstructive defects of renal pelvis and ureter (dilated uropathy grade II-IV/ureterocele)	30	17.7	19.2
	Q25.0	Persistant Ductus Botalli (hemodynamically effective)	30	17.7	6.9
4.	Q90.	Down's Syndrome (Trisomy 21)	27	15.9	16.7
5.	Q66.0	Talipes equinovarus (clubfoot)	24	14.1	18.8
6.	H90.	Conductive and sensorineural hearing loss	23	13.5	6.4 (15.1*)
7.	Q69.	Polydactyly (pre- und postaxial)	22	12.9	11.6
8.	Q54.1 Q54.2 Q54.3 Q54.8 Q54.9	Hypospadias (without coronal/glandular)	16	9.4	7.3
9.	Q62.1	Atresia and stenosis of ureter	15	8.8	7.0
10.	Q02.	Microcephaly	13	7.7	11.4
	Q37.	Cleft hard and soft palate with unilateral/bilateral cleft lip	13	7.7	11.3
	Q22.1	Pulmonary valve stenosis	13	7.7	5.8
11.	Q60.0	Renal agenesia (unilateral)	12	7.1	6.9
	Q62.2	Congenital megaureter	12	7.1	6.6
12.	Q61.4	Renal dysplasia/Potter II	11	6.5	5.6
	Q65.3 Q65.4 Q65.5	Congenital subluxation of hip (unilateral/bilateral/laterality unspecified)	11	6.5	18.1
13.	Q25.1	Coarctation of aorta	8	4.7	4.6
	Q42.2 Q42.3	Congenital absence, atresia and stenosis of anus with or without fistula	8	4.7	4.1
	Q79.3	Gastrochisis	8	4.7	3.8
	Q20.3	Discortant ventriculoaterial connection (inclusive complete TGV)	8	4.7	3.5
	Q25.6	Stenosis of pulmonary artery peripheral pulmonary valve stenosis)	8	4.7	1.8
	Q03.0 Q03.1 Q03.8 Q03.9	Congenital hydrocephalus without neural tube defect	8	4.7	6,1

* 2007-2010 (since 2007 data synchronization with newborn hearing screening tracking centre)

12 Indicator Defects of the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR)

12.0 Definitions

1. Neural tube defects: common congenital malformations that occur when the neural tube fails to achieve proper closure during early embryogenesis, resulting in defective development of the associated vertebral arches. Synonyms: Spina bifida, anencephaly, NTD

2. Anencephaly: a congenital malformation characterized by the total or partial absence of the cranial vault, the covering skin, and the brain missing or reduced to small mass. Inclusive craniorachischisis. Inclusive infants with iniencephaly and other neural tube defects as Encephalocele or open spina bifida, when associated with anencephaly.Exclusive acephaly, that is, absence of head observed in amorphous acardiac twins.

3. Spina bifida: a family of congenital malformation defects in the closure of the spinal column characterized by herniation or exposure of the spinal cord and/or meges through an incompletely closed spine. Inclusive meningocele, meningomyelocele, myelocele, myelomeningocele, rachischisis. Spina bifida is not counted when present with anencephaly. Exclusive spina bifida occulta, sacrococcygeal teratoma without dysraphism.

4. Encephalocele: a congenital malformation characterized by herniation of the brain and/or meninges through a defect in the skull. Encephalocele is not counted when present with spina bifida.

5. Microcephaly: a congenitally small cranium, defined by an occipito frontal circumference (OFC) 3 standard deviation below the age and sex appropriate distribution curves.[If using a different definition or cut off point (e.g., 2 standard deviations), report but specify criteria]. Exclusive microcephaly associated with anencephaly or encephalocele

6. Congenital Hydrocephaly: a congenital malformation characterized by dilatation of the cerebral ventricles, not associated with a primary brain atrophy, with or without enlargement of the head, and diagnosed at birth. Not counted when present with encephalocele or spina bifida. Exclusive macrocephaly without dilatation of ventricular system, skull of macerated fetus, hydranencephaly, holoprosencephaly, and postnatally acquired hydrocephalus.

7. Arhinencephaly/Holoprosencephaly: a congenital malformation of the brain, characterized by various degrees of incomplete lobation of the brain hemispheres. Olfactory nerve tract may be absent. Holoprosencephaly includes cyclopia, ethmocephaly, cebocephaly, and premaxillary agenesis.

8. Anophthalmos/Microphthalmos: apparently absent or small eyes. Some normal adnexal elements and eyelids are usually present. In microphthalmia, the corneal diameter is usually less than 10 mm. and the antero posterior diameter of the globe is less than 20 mm.

9. Anotia/Microtia: a congenital malformation characterized by absent parts of the pinna (with or without atresia of the ear canal) commonly expressed in grades (I - IV) of which the extreme form (grade V) is anotia, absence of pinna. Exclusive small, normally shaped ears, imperforate auditory meatus with a normal pinna, dysplastic and low set ears.

10. Tetralogy of Fallot: a condition characterized by ventricular septal defect, overriding aorta, infundibular pulmonary stenosis, and often right ventricular hypertrophy.

11. Transposition of great vessels (TGV): a cardiac defect where the aorta exits from the right ventricle and the pulmonary artery from the left ventricle, with or without other cardiac defects. Inclusive double outlet ventricle so called corrected transposition.

12. Hypoplastic left heart sydrome: a cardiac defect with a hypoplastic left ventricle, associated with aortic and/or mitral valve atresia, with or without other cardiac defect.

13. Coarctation of the aorta: an obstruction in the descending aorta, almost invariably at the insertion of the ductus arteriosus.

14. Cleft lip with or without cleft palate : a congenital malformation characterized by partial or complete clefting of the upper lip, with or without clefting of the alveolar ridge or the hard palate. Exclusive midline cleft of upper or lower lip and oblique facial fissure (going towards the eye).

15. Cleft palate without cleft lip : a congenital malformation characterized by a closure defect of the hard and/or soft palate behind the foramen incisivum without cleft lip. Inclusive submucous cleft palate. Exclusive cleft palate with cleft lip, cleft uvula, functional short palate, and high narrow palate.

16. Choanal atresia, bilateral: congenital obstruction (membraneous or osseous) of the posterior choana or choanae. Exclusive choanal stenosis and congestion of nasal mucosa.

17. Oesophageal atresia/stenosis: a congenital malformation characterized by absence of continuity or narrowing of the esophagus, with or without tracheal fistula. Inclusive Tracheoesophageal fistula with or without mention of atresia or stenosis of oesophagus.

18. Small intestine atresia/stenosis: complete or partial occlusion of the lumen of a segment of the small intestine. It can involve a single area or multiples areas of the jejunum or ileum. Exclusive duodenal atresia.

19. Anorectal atresia/stenosia: a congenital malformation characterized by absence of continuity of the anorectal canal or of communication between rectum and anus, or narrowing of anal canal, with or without fistula to neighboring organs. Exclusive mild stenosis which does not need correction, and ectopic anus.

20. Undescended testis: bilateral undescended testes in at term newborn or at least unilateral undescended testis in males more than 1 year of age. Exclusive retractrile testis.

21. Hypospadias: a congenital malformation characterized by the opening of the urethra on the ventral side of the penis, distally to the sulcus. Incl. penile, scrotal, and perineal hypospadias. Exclusive glandular or first degree hypospadias and ambiguous genitalia (intersex or pseudohermaphroditism).

22. Epispadias a congenital malformation characterized by the opening of the urethra on the dorsal surface of the penis. Not counted when part of exstrophy of the bladder.

23. Indeterminate sex: genital ambiguity at birth that does not readily allow for phenotypic sex determination. Incl. male or female true or pseudohermaphroditism.

24. Potter sequence: a congenital malformation characterized by complete absence of kidneys bilaterally or severely dysplastic kidneys.

25. Renal agenesis, unilateral: a congenital malformation characterized by complete absence of one kidney unilaterally. Exclusive unilateral dysplastic kidney.

26. Cystic kidney: a congenital malformation characterized by multiple cysts in the kidney. Inclusive infantile polycystic kidney, multicystic kidney, other forms of cystic kidney and unspecified cystic kidney. Exclusive single kidney cyst.

27. Bladder exstrophy: complex malformation characterized by a defect in the closure of the lower abdominal wall and bladder. Bladder opens in the ventral wall of the abdomen between the umbilicus and the symphysis pubis. It is often associated with epispadias and structural anomalies of the pubic bones.

28. Polydactyly, preaxial: extra digit(s) on the radial side of the upper limb or the tibial side of the lower limb. It can affect the hand, the foot, or both.

29. Limb reduction defects: a congenital malformation characterized by total or partial absence or severe hypoplasia of skeletal structures of the limbs. Inclusive femoral hypoplasia. Exclusive mild hypoplasia with normal shape of skeletal parts, brachydactyly, finger or toe reduction directly associated with syndactyly, general skeletal dysplasia and sirenomelia.

30. Diaphragmatic hernia: a congenital malformation characterized by herniation into the thorax of abdominal contents through a defect of the diaphragm. Inclusive total absence of the diaphragm. Exclusive hiatus hernia, eventration and phrenic palsy.

31. Omphalocele: a congenital malformation characterized by herniation of abdominal contents through the umbilical insertion and covered by a membrane which may or may not be intact. Exclusive gastroschisis (para umbilical hernia), a or hypoplasia of abdominal muscles, skin covere umbilical hernia.

32. Gastroschisis: a congenital malformation characterized by visceral herniation through a right side abdominal wall defect to an intact umbilical cord and not covered by a membrane. Exclusive a or hypoplasia of abdominal muscles, skin covered umbilical hernia, omphalocele.

33. Prune belly sequence: a complex congenital malformation characterized by deficient abdominal muscle and urinary obstruction/distension. It can be caused by urethral obstruction secondary to posterior urethral valves or urethral atresia. In the affected fetus the deficiency of the abdominal muscle may not be evident. It can be associated with undescended testes, clubfoot, and limb deficiencies.

34. Down's syndrome (Trisomy 21): a congenital chromosomal malformation syndrome characterized by a well known pattern of minor and major anomalies and associated with excess chromosomal 21 material. Inclusive trisomy mosaicism and translocations of chromosome 21.

35. Patau syndrome (Trisomy 13): a congenital chromosomal malformation syndrome associated with extra chromosome 13 material. Inclusive translocation and mosaic trisomy 13.

36. Edward's syndrome (Trisomy 18): a congenital chromosomal malformation syndrome associated with extra chromosome 18 material. Inclusive translocation and mosaic trisomy 18.

Note:

The prevalences we calculated in the following chapters are population based. The value indicates the number of birth with malformations born in a certain population with reference to the total number of birth in his population. Since 2000 the prevalence calculations are only referring to children whose mothers have their residence in Saxony-Anhalt. Between 1997-1999 the registration area of the Monitoring of Congenital Malformations did not cover the entire area of Saxony-Anhalt. (1997: 14, 1998: 15, 1999: 16 out of 21 administrative districts). The calculation of the basic prevalences is based on a total number of 205,635 birth.

The analysis of the indicator malformations is made with regard to the diagnoses. It is possible that one child has more than one indicator malformation. Therefore the number of all indicator malformations can be higher than the total number of birth with an indicator malformation.

12.1 Neural tube defects (Q00./Q01./Q05.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities 1 x Halle	1	2.1	↓
Districts: 1 x Anhalt-Bitterfeld 1 x Börde 1 x Saalekreis 1 x Salzlandkreis 1 x Wittenberg	5	4.1	↓
Saxony-Anhalt	**6**	**3.5**	↓

Neural tube defects (1999-2010)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	10.45	7.83 - 13.66
Districts	9.49	8.11 - 11.09
Region	9.73	8.49 - 11.13
EUROCAT	9.82	4.67 S Portugal* 18.16 Mainz (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

In 2011 we registered 6 neural tube defects in Saxony-Anhalt. The resulting **prevalence** of **3.5 per 10,000 births** was lower than the prevalence of the last years and represents the lowest value we observed since 1999.

Compared to EUROCAT the annual prevalence is as well lower as the European basic prevalence and at the same time the lowest basic prevalence that was ever registered by the European centres.

additional information:

Pregnancy outcome	2 x live birth 4 x termination of pregnancy
Sex	1 x male 4 x female 1 x no information
Number of isolated malformations/MCA	2 x MCA 4 x isolated

The sex ratio of births with NTDs shows that mainly female infants were affected.

In regard to the pregnancy outcome the figures show that in 67% of the cases a termination of pregnancy was induced. The reason not to continue with the pregnancy was the finding of the prenatal ultrasound screening. In one case an anencephaly was diagnosed, in three cases an encephalocele was detected prenatally. 33% of infants with a neural tube defect were live births in 2011. In these cases a spina bifida was diagnosed.

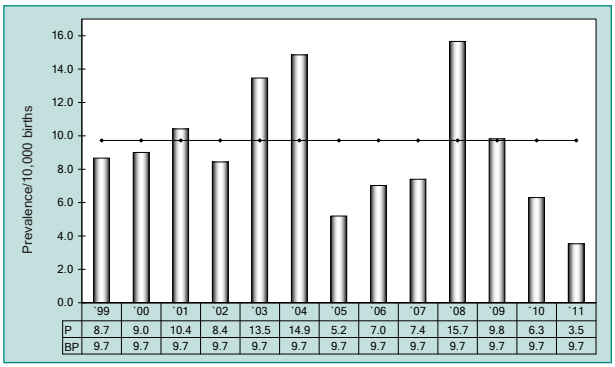


Fig. 6: Development of prevalence/10,000 births with neural tube defects in the registration area since 1999

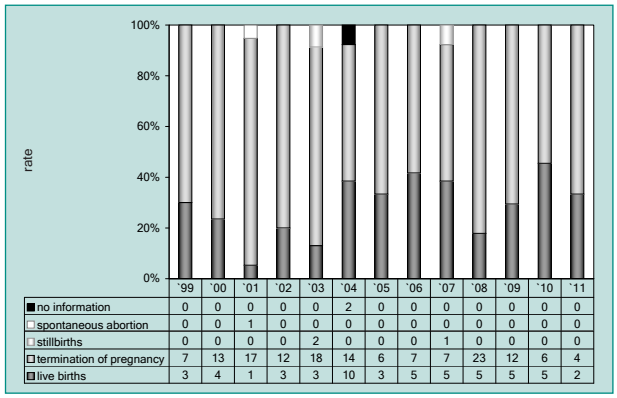


Fig. 7: Pregnancy outcomes of neural tube defects in the registration area since 1998

In 2011 one neural tube defect per 2832 births was registered in Saxony-Anhalt.

12.2 Anencephalie (Q00.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities	0	0.0	↓
Districts: 1 x Börde	1	0.8	↓
Saxony-Anhalt	**1**	**0.6**	↓

Anencephalie (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	1.38	0.55 - 2.84
Districts	2.58	1.84 - 3.52
Region	2.29	1.68 - 3.04
EUROCAT	3.68	1.68 Tuscany (Italy)* 7.46 Ukraine**

*/** centres with lowest resp. highest prevalence/10,000 births

Only one birth with anencephaly was registered in 2011. This corresponds to a prevalence of 0.6 per 10,000 births. A similar low annual prevalence was observed in 2006. When comparing the annual prevalences of the last years we registered very high prevalences (e.g. 2008: 5.0 per 10,000 births) as well as very low prevalences (current value in 2011).

In the European comparison the current annual prevalence of Saxony-Anhalt is lower than the European reference values.

additional information:

Pregnancy outcome	1 x termination of pregnancy
Sex	1 x female
Number of isolated malformations/MCA	1 x isolated

The female infant with anencephaly originated from the district Bördekreis. The pregnancy was terminated after 12 weeks of gestation, reason was a TRAP sequence (Twin Reversed
Arterial Perfusion). In these cases the upper half of the body of one twin is underperfused due to a monochorionic placenta which leads among others to the above mentioned malformation.

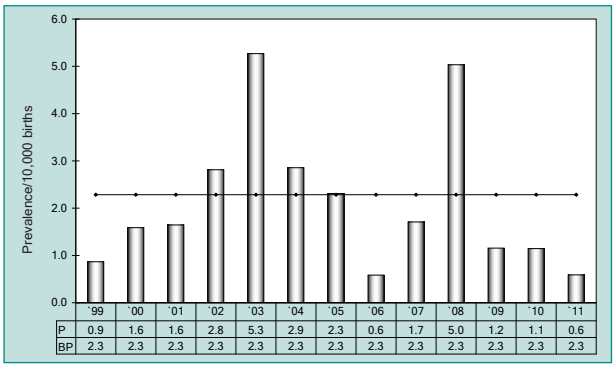


Fig. 8: Development of prevalence/10,000 births with anencephaly in the registration area since 1999

In 2011 one anencephaly per 16,989 births was registered in Saxony-Anhalt.

12.3 Spina bifida (Q05.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities	0	0.0	↓
Districts: 1 x Anhalt-Bitterfeld 1 x Saalekreis	2	1.6	↓
Saxony-Anhalt	**2**	**1.2**	↓

Spina bifida (1999-2010)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	6.70	4.64 - 9.36
Districts	5.94	4.79 - 7.28
Region	6.13	5.17 - 7.25
EUROCAT	5.00	1.92 Zagreb (Croatia)* 11.05 Mainz (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

In 2011 two births with spina bifida were registered in Saxony-Anhalt.
The **prevalence** of **1.2 per 10,000 births** is the lowest annual prevalence of this malformation we observed during the last years. The annual prevalence also lies under the confidence interval of 1999 to 2010.

Compared to European data records our prevalence of 2011 is to be classified rather low as it also lies under the basic prevalence that has been calculated by EUROCAT.

additional information:

Pregnancy outcome	2 x live birth
Sex	1 x male 1 x female
Number of isolated malformations/MCA	1 x MCA 1 x isolated

The sex ratio is balanced.

Both infants with spina bifida were born alive and punctually. We have no indication about prenatal diagnoses or intake of folic acid before and during pregnancy in both cases.

The two infants suffered from a sacral spina bifida without hydrocephaly.

Malformation combinations (MCA) or superordinated syndromes detected:

- tethered cord syndrome, subcutan lipom

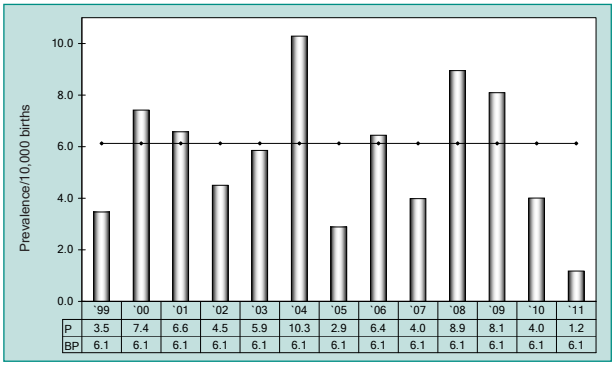


Fig. 9: Development of prevalence/10,000 births with spina bifida in the registration area since 1999

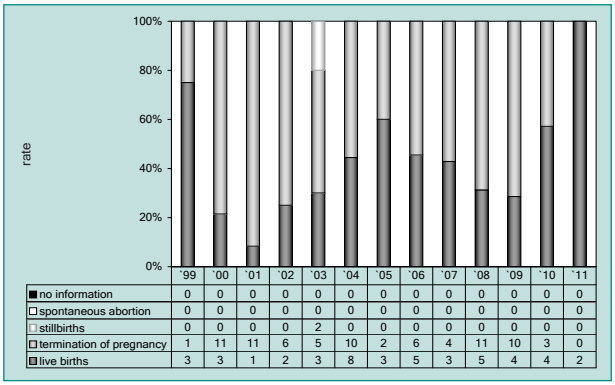


Fig. 10: Pregnancy outcomes of spina bifida in the registration area since 1999

In 2011 one spina bifida per 8495 births was registered in Saxony-Anhalt.

12.4 Encephalocele (Q01.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle	1	2.1	↔
Districts: 1 x Salzlandkreis 1 x Wittenberg	2	1.6	↗
Saxony-Anhalt	**3**	**1.8**	↔

Encephalocele (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	2.37	1.22 - 4.13
Districts	0.97	0.54 - 1.60
Region	1.31	0.87 - 1.91
EUROCAT	1.14	0.39 S Portugal* 3.16 Mainz (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

Three births with encephalocele were registered in 2011. The prevalence of 1.8 per 10,000 births remains in comparison to the previous years unchanged and lies within the range of the confidence interval of the years 1999-2010.

Compared with European data the prevalence is at the middle range. In all three cases of encephalocele the termination of pregnancy was induced after 19 or 20 weeks of gestation.

additional information:

Pregnancy outcome	3 x termination of pregnancy
Sex	2 x female 1 x no information
Number of isolated malformations/MCA	1 x MCA 2 x isolated

In one case the complex malformation syndrome VACTERL association was present.

Malformation combinations (MCA) or superordinated syndromes detected:

- VACTERL association with: cleft of the hard palate, renal agenesis right, cleft hand left, clubhand with missing thumb and radius right, hypoplastic ulna right, hypoplastic gallbladder, missing cervical vertebra, multiple hemivertebra, butterfly vertebra and fusion of hemivertebra, missing ribs bilateral, hypoplastic aorta, malformation of the right upper eyelid, low-set right ear

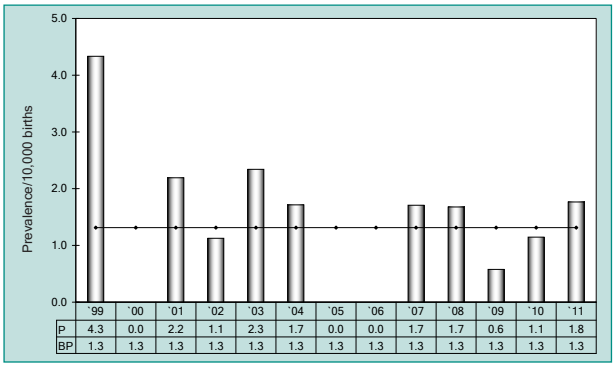


Fig 11: Development of prevalence/10,000 births with encephalocele in the registration area since 1999

In 2011 one encephalocele per 5663 births was registered in Saxony-Anhalt.

12.5 Microcephaly (Q02.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle 7 x Magdeburg	8	16.7	↗
Districts: 1 x Anhalt-Bitterfeld 3 x Harz 1 x Salzlandkreis	5	4.1	↓
Saxony-Anhalt	**13**	**7.7**	↓

Microcephaly (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	13.01	10.07 - 16.55
Districts	10.72	9.24 - 12.41
Region	11.28	9.95 - 12.78
EUROCAT	2.35	0.49 Norway* 11.28 Saxony-Anhalt (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

13 births with microcephaly were registered in 2011. These births were registered as they had a head circumference below the 3rd percentile in regard to the gestational age or a corresponding head circumference at birth. The **prevalence** of **7.7 per 10,000 births** is altogether lower than the basic prevalence of the years 1999-2010. The prevalence in the major cities of 16.7 per 10,000 births ranges above the confidence interval. The current prevalence is lower than in the previous years but ranges at the same level of 2008.

In comparison to the EUROCAT data Saxony-Anhalt ranges in the middle.

additional information:

Pregnancy outcome	8 x live birth 2 x spontaneous abortion 3 x stillbith
Sex	8 x male 5 x female
Number of isolated malformations/MCA	4 x MCA 9 x isolated

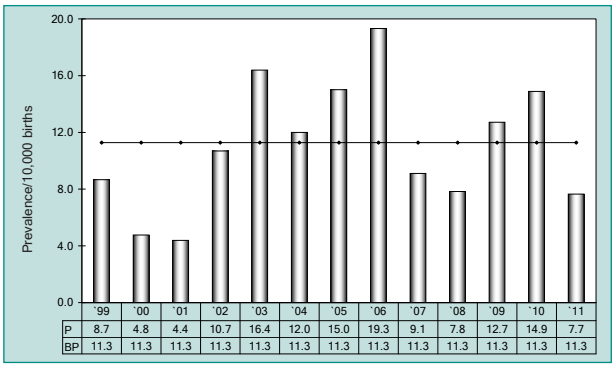
The sex ratio shows that mainly male infants/foetuses were affected.

Altogether, we registered eight life births. In two cases spontaneous abortions were reported, one after 25 and another after 26 weeks of gestation. The reason was placental insufficiency. We registered three stillbirths, the reasons were in two cases placental insufficiency and in one case an umbilical cord strangulation.

Additional malformations within a MCA or superordinated syndrome occurred in only four cases. We registered such combinations more often in the previous years.

Malformation combinations (MCA) or superordinated syndromes detected:

- Down's syndrome with: DUP III. grade blt., megaureter left
- small intestine stenosis, PFO and haemodynamic not relevant PDA at preterm birth
- PFO and haemodynamic relevant PDA at preterm birth
- single cerebral cyst right, single transverse palmar crease blt., sandal's gap blt., mandibular retrognathia



	`99	`00	`01	`02	`03	`04	`05	`06	`07	`08	`09	`10	`11
P	8.7	4.8	4.4	10.7	16.4	12.0	15.0	19.3	9.1	7.8	12.7	14.9	7.7
BP	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3

Fig. 12: Development of prevalence/10,000 births with hydrocephaly in the registration area since 1999

In 2011 one microcephalus per 1307 births was registered in Saxony-Anhalt.

12.6 Congenital Hydrocephaly (Q03.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 2 x Halle 2 x Magdeburg	4	8.4	↔
Districts: 1 x Burgenlandkreis 1 x Harz 1 x Jerichower Land 1 x Salzlandkreis	4	3.3	↓
Saxony-Anhalt	**8**	**4.7**	↓

Congenital Hydrocephaly (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	7.29	5.14 - 10.05
Districts	5.75	4.61 - 7.07
Region	6.13	5.17 - 7.25
EUROCAT	5.66	2.05 Dublin (Ireland)* 13.14 Paris (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

Eight births with congenital hydrocephalus were registered in 2011. Please note that the hydrocephalus which occurred in combination with spina bifida resp. encephalocele is not regarded here. Also the hydrocephalus that appeared postnatal is not included in this analysis.
The **prevalence** lies at **4.7 per 10,000 births** and ranges altogether and in the districts under the basic prevalence of 1999-2010. The trend only remained unchanged in the major cities Halle and Magdeburg with two registered cases.

Compared to the European data the frequency registered in Saxony-Anhalt is within the lower range.

additional information:

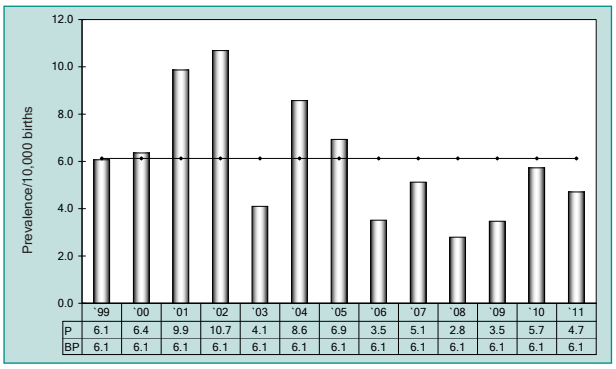
Pregnancy outcome	8 x live birth
Sex	4 x male 4 x female
Number of isolated malformations/MCA	3 x MCA 5 x isolated

All infants were born alive. The sex ratio is balanced. The pregnancy anamnesis of the persons concerned showed former fertility treatment, abuse, status after more than two spontaneous abortions or terminations of pregnancy, family predisposition with congenital malformations as well as gestational diabetes and coagulopathy. In four cases the diagnoses was made already prenatally.

MCA or superordinated syndromes occurred in three cases.

Malformation combinations (MCA) or superordinated syndromes detected:

- Arnold-Chiari-syndrome with: postductal coarctation of aorta, aplasia of the evator anguli oris right, haemodynamic relevant PDA at full term infant, DUP I. grade bil.
- hydranencephaly, cerebellar hypoplasia, renal hypoplasia bil., arachnodactyly (of fingers), sacral dimple, macrocephaly, hemangioma at the upper lip
- PFO at full term infant, membranous accessory finger (postminimus) left



	`99	`00	`01	`02	`03	`04	`05	`06	`07	`08	`09	`10	`11
P	6.1	6.4	9.9	10.7	4.1	8.6	6.9	3.5	5.1	2.8	3.5	5.7	4.7
BP	6.1	6.1	6.1	6.1	6.1	6.1	6.1	6.1	6.1	6.1	6.1	6.1	6.1

Fig. 13: Development of prevalence/10,000 births with congenital hydrocephalus in the registration area since 1999

In 2011 one congenital hydrocephalus per 2124 births was registered in Saxony-Anhalt.

12.7 Arhinencephaly/Holoprosencephaly (Q04.1/Q04.2)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Magdeburg	1	2,1	↔
Districts	0	0,0	↓
Saxony-Anhalt	**1**	**0,6**	↓

Arhinencephaly/Holoprosencephaly (1999-2010)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	2,56	1,36 - 4,38
Districts	1,23	0,74 - 1,92
Region	1,56	1,06 - 2,20
EUROCAT	1,30	0,35 Wielkopolska (Poland)* 2,88 Ukraine**

*/** centres with lowest resp. highest prevalence/10,000 births

In 2011 one birth with holoprosencephaly was registered in the major city of Magdeburg. This corresponds to a **prevalence** of **0.6 per 10,000 births**. Compared to the figures of the previous years, the frequency of appearance differs very much. The annual prevalence 2011 ranges under the basic prevalence of 1999-2010 and also lies under the confidence interval.

In the previous years the frequency of appearance of arhinencephaly/holoprosencephaly changed regularely.

In comparison with the European centers the registered value is rather low this year.

additiional information:

Pregnancy outcome	1 x live birth descended within 7 days of life
Sex	1 x male
Number of isolated malformations/MCA	1 x MCA

The male preterm infant with above mentioned malformation was delivered after 30 weeks of gestation and a birth weight of 860g. It deceased two hours later due to his numerous malformations.

Malformation combinations (MCA) or superordinated syndromes detected:

- Potter sequence (renal agenesia bilateral), missing nasal septum, malformation of pharynx, shortened upper and lower limbs bil.

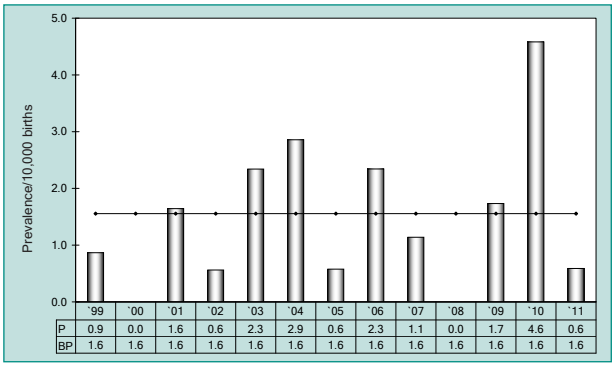


Fig. 14: Development of prevalence/10,000 births with arhinencephalie/holoprosencephalie in the registration area since 1999

In 2011 one case of arhinencephalie/holoprosencephalie per 16,989 births was registered in Saxony-Anhalt.

12.8 Anophthalmos/Microphthalmos (Q11.0/Q11.1/Q11.2)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle	1	2,1	↔
Districts	0	0,0	↓
Saxony-Anhalt	**1**	**0,6**	↔

Anophthalmos/Microphthalmos (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	1,38	0,55 - 2,84
Districts	0,58	0,27 - 1,10
Region	0,78	0,44 - 1,26
EUROCAT	1,00	0,13 Zagreb (Croatia)* 3,27 Odense (Denmark)**

*/** centres with lowest resp. highest prevalence/10,000 births

One female live birth with anophthalmos was registered in Halle in 2011. The prevalence is with a value of 0.6 per 10,000 births within the lower range of the confidence interval 1999-2010.

Also in comparison to the EUROCAT data the prevalence of 2011 occupies a position in the lower area.

additiional information:

Pregnancy outcome	1 x live birth
Sex	1 x female
Number of isolated malformations/MCA	1 x MCA

The infant with anophthalmia was born by a 25 years old woman. The pregnancy anamnesis indicated a nicotine abuse. The child suffers from additional malformation of the heart and kidneys which can be united to a MCA.

Malformation combinations (MCA) or superordinated syndromes detected:

- optic atrophy blt., malformation of vitreous, microcornea und cataract blt., ASD II, PFO at full term infant, duplex kidney left, hearing loss n.o.s. left, renal hypoplasia blt., shortened palpebral fissure bil.

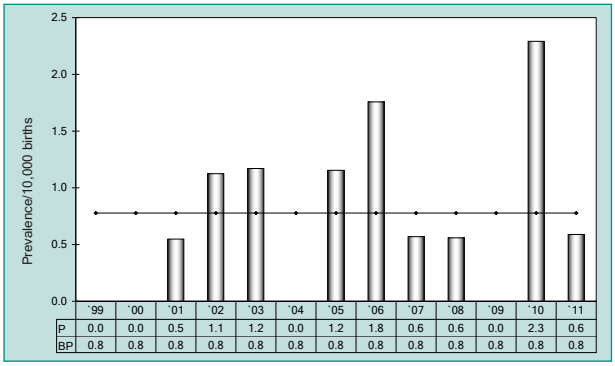


Fig. 15: Development of prevalence/10,000 births with anophthalmos/microphthalmos in the registration area since 1999

In 2011 one child with anophthalmos/microphthalmos per 16,989 births was registered in Saxony-Anhalt.

12.9 Microtia/Anotia (Q16.0/Q17.2)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities	0	0,0	↓
Districts: 1 x Mansfeld-Südharz	1	0,8	↘
Saxony-Anhalt	1	0,6	↓

Microtia/Anotia (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	1,77	0,81 - 3,37
Districts	1,36	0,84 - 2,07
Region	1,46	0,98 - 2,08
EUROCAT	no informationn	no informationn

In 2011 we registered one case of anotia. Therefore, this rarely appearing malformation has a prevalence of 0.6 per 10,000 births. This value ranges under the basic prevalence that has to be expected.

This rarely appearing malformation is not analyzed by EOROCAT.

additiional information:

Pregnancy outcome	1 x live birth
Sex	1 x female
Number of isolated malformations/MCA	1 x MCA

The affected female infant was born in the district Mansfeld-Südharz. Addditional malformations occurred mainly at fingers and toes of the child and can be classified as MCA.

Malformation combinations (MCA) or superordinated syndromes detected:

- missing finger right, amniotic strangulation mark at right fingers and toes bil., overlapping toes bil., single transverse palmar crease right

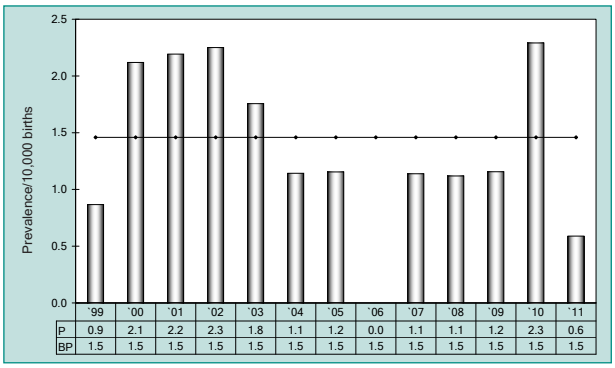


Fig. 16: Development of prevalence/10,000 births with microtia/anotia in the registration area since 1999

In 2011 one child with microtia/anotia per 16,989 was registered in Saxony-Anhalt.

12.10 Tetralogy of Fallot (Q21.3)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle	1	2,1	↔
Districts: 1 x Anhalt-Bitterfeld	1	0,8	↓
Saxony-Anhalt	**2**	**1,2**	↓

Tetralogy of Fallot (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	3,15	1,80 - 5,12
Districts	3,42	2,56 - 4,47
Region	3,36	2,16 - 4,25
EUROCAT	3,16	2,04 S Portugal* 6,28 Northern England (UK)**

*/** centres with lowest resp. highest prevalence/10,000 births

The occurence of tetralogy of fallot was reported in two cases in 2011. The prevalence of 1.2 per 10,000 births ranges under the prevalences of the previous years. In 2000 and 2007 a similar low prevalence was registered.

Also in comparison with European data, the value from Saxony-Anhalt occupies a position underneath the confidence interval.

additiional information:

Pregnancy outcome	2 x live birth
Sex	1 x male 1 x female
Number of isolated malformations/MCA	1 x MCA 1 x isolated

The infants with tetralogy of fallot were born after 39 and 40 weeks of gestation. In one case the diagnosis was confirmed prenatally and the delivery took place in a center for perinatal care.

Malformation combinations (MCA) or superordinated syndromes detected:

- PFO at full term infant

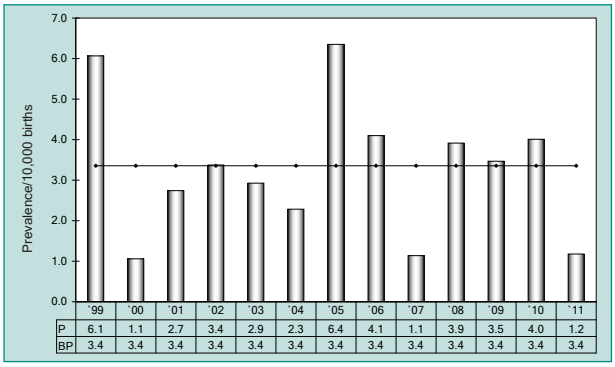


Fig. 17 Development of prevalence/10,000 births with tetralogy of fallot in the registration area since 1999

In 2011 one tetralogy of fallot per 8495 births was registered in Saxony-Anhalt.

12.11 Transposition of Great Vessels - TGV (Q20.1/Q20.3)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 3 x Halle	3	6,3	↔
Districts: 1 x Altmarkkreis Salzwedel 2 x Anhalt-Bitterfeld 1 x Harz 1 x Mansfeld-Südharz 1 x Saalekreis 1 x Salzlandkreis	7	5,7	↗
Saxony-Anhalt	**10**	**5,9**	↗

Transposition of Great Vessels (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	5,32	3,51 - 7,74
Districts	4,07	3,13 - 5,20
Region	4,38	3,52 - 5,38
EUROCAT (Q20.3)	3,38	1,36 S Portugal* 5,32 Barcelona (Spain)**

*/** centres with lowest resp. highest prevalence/10,000 births

We registered ten births with TVG in Saxony-Anhalt in 2011. The **prevalence** of **5.9 per 10,000 births** ranges above the prevalence we registered in the previous years and shows a value which is also higher than the basic prevalence of 1999-2010. Seven of the affected infants were registered in the districts.

In comparison with European centres the value from Saxony-Anhalt lies above the confidence interval.

additiional information:

Pregnancy outcome	10 x live birth
Sex	9 x male 1 x female
Number of isolated malformations/MCA	9 x MCA 1 x isolated

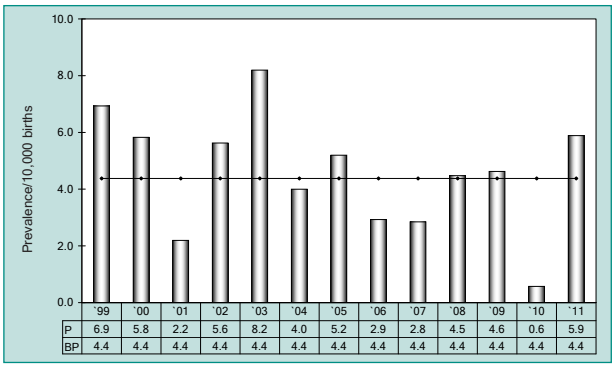
The sex ratio shows a clear androtropism as nine male infants and only one female infant suffered from TVG.

All infants were born in time and alive. Nine children had beside a TVG additional and mainly cardiac malformations.

We received a report of the prenatal diagnoses TVG only in three cases.
Five infants were deliverd in centres of perinatal care. A huge challenge in such cases is the procedure from diagnosing the congenital heart defect to moving the infant, partially via paediatric clinics, to a paediatric cardiology where the appropiate care can be offered.

Malformation combinations (MCA) or superordinated syndromes detected:

- VSD, hypoplastic aorta, pulmonary valve stenosis, PFO at full term infant
- VSD, hypoplastic aorta, pulmony valve insufficiency, PFO at full term infant
- VSD, PFO at full term infant, malformation of coronary vessels
- VSD, PFO at full term infant
- 2 x ASD II and malformation of coronary vessels
- ASD, PFO at full term infant
- ASD II
- PFO at full term infant



	'99	'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11
P	6.9	5.8	2.2	5.6	8.2	4.0	5.2	2.9	2.8	4.5	4.6	0.6	5.9
BP	4.4	4.4	4.4	4.4	4.4	4.4	4.4	4.4	4.4	4.4	4.4	4.4	4.4

Fig. 18: Development of prevalence/10,000 births with transposition of great vessels in the registration area since 1999

In 2011 one transposition of great vessels per 1699 births was registered in Saxony-Anhalt.

12.12 Hypoplastic Left Heart Syndrome (Q23.4)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Dessau-Roßlau 1 x Halle	2	4,2	↔
Districts: 1 x Börde 1 x Harz	2	1,6	↓
Saxony-Anhalt	**4**	**2,4**	↔

Hypoplastic Left Heart Syndrome (1999-2010)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	2,56	1,36 - 4,38
Districts	3,23	2,40 - 4,25
Region	3,06	2,35 - 3,92
EUROCAT	2,65	1,27 S Portugal* 4,28 Styria (Austria)**

*/** centres with lowest resp. highest prevalence/10,000 births

The hypoplastic left heart syndrome was registered in four cases in 2011 and has therefore a value that is within the basic prevalence. We calculated a **prevalence** of **2.4 pro 10,000 births** and get a value which is within the confidence intrval of the previous years.

Compared to EUROCAT centres the prevalence of Saxony-Anhalt is within the middle range.

additiional information:

Pregnancy outcome	1 x live birth 1 x live birth descended within 7 days of life 2 x termination of pregnancy
Sex	2 x male 1 x female 1 x no information
Number of isolated malformations/MCA	3 x MCA 1 x isolated

In two cases a termination of pregnancy took place after 21 weeks of gestation because the diagnosis of hypoplastic left heart syndrome was prenatally confirmed. Two infants were delivered in time and alive. They were moved to a paediatric cardiology, however one infant deceased within the first 7 days of life.

The hypoplastic left heart syndrome appeared in three cases in combination with other malformations.

Malformation combinations (MCA) or superordinated syndromes detected:

- ASD II, bronchial stenosis left, diaphragmatic paralysis right, pes adductus right
- mitral valve stenosis, alasia cutis congenita of pericranium
- segmentation defect (additional groove) of lung bil

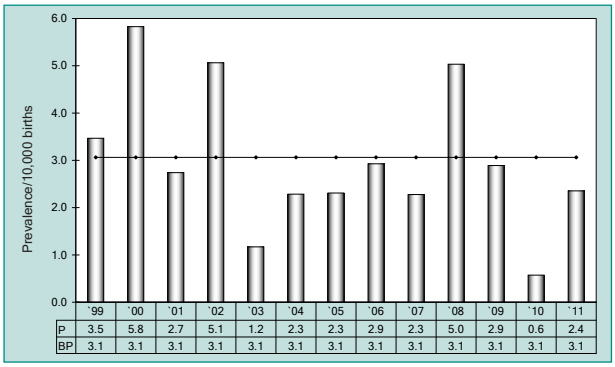


Fig. 19: Development of prevalence/10,000 births with hypoplastic left heart syndrome in the registration area since 1999

In 2011 one child with a hypolastic left heart syndrome per 4247 births was registered in Saxony-Anhalt.

12.13 Coarctation of Aorta (Q25.1)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Magdeburg	1	2,1	↓
Districts: 1 x Börde 3 x Harz 2 x Salzlandkreis 1 x Wittenberg	7	5,7	↗
Saxony-Anhalt	**8**	**4,7**	↔

Coarctation of Aorta (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	5,13	3,35 - 7,51
Districts	4,26	3,30 - 5,42
Region	4,47	3,61 - 5,49
EUROCAT	1,26	0,16 S Portugal* 3,38 Vaud (Switzerland)**

*/** centres with lowest resp. highest prevalence/10,000 births

In 2011 we registered eight births with coarctation of aorta. The corresponding prevalence of 4.7 per 10,000 births lies is within the middle range of the basic prevalence of 1999-2010. We have to state that the number of infants with coarctation of aorta increased only in the districts.

A prevalence of 1.26 per 10,000 births is calculated by the EUROCAT centres. The value we registered in Saxony-Anhalt exceeds this prevalence.

additiional information:

Pregnancy outcome	8 x live birth
Sex	5 x male 3 x female
Number of isolated malformations/MCA	6 x MCA 2 x isolated

All eight infants were born between 28 and 41 weeks of gestation. The sex ratio shows an androtropism.

In no case we have information about prenatal ultrasound screening results. In two cases with positive family history the infants were not delivered in a centre of perinatal care, i.e. no prenatal findings were conspicuous.

The combination with additional malformations or superordinated syndroms appeared in six cases, in five of these cases the infants suffered from heart malformations.

Malformation combinations (MCA) or superordinated syndromes detected:

- Arnold-Chiari-syndrome with: hydrocephalus internus, aplasia of levator anguli oris right, haemodynamic relevant PDA at full term infant, DUP I. grade bil.
- VSD, ASD, PFO at preterm infant, haemangioma
- ASD II, retarded hip
- ASD II
- PFO und haemodynamic effective PDA at full term infant, lateral ascending eyelids bil.
- PFO at full term infant

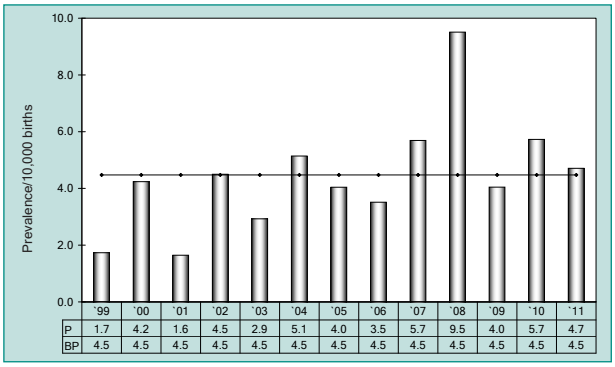


Fig. 20: Development of prevalence/10,000 births with coarctation of aorta in the registration area since 1999

In 2011 one coarctation of aorta per 2124 births was registered in Saxony-Anhalt.

12.14 Cleft Lip With or Without Cleft Palate (Q36./Q37.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 2 x Halle 2 x Magdeburg	4	8,4	↓
Districts: 1 x Anhalt-Bitterfeld 3 x Börde 2 x Harz 2 x Jerichower Land 2 x Mansfeld-Südharz 2 x Saalekreis 1 x Stendal	13	10,7	↓
Saxony-Anhalt	**17**	**10,0**	↓

Cleft Lip With or Without Cleft Palate (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	15,18	11,98 - 18,96
Districts	14,78	13,03 - 16,76
Region	14,88	13,33 - 16,60
EUROCAT	9,02	4,33 S Portugal* 14,32 Odense (Denmark)**

*/** centres with lowest resp. highest prevalence/10,000 births

17 births with cleft lip with or without cleft palate were registered in 2011. In comparison to the previous yeras the number of affected births can be classified this year as rather low. The prevalence of 10.0 per 10,000 births is clearly under the confidence interval of 1999-2010, in total as well as in the districts and major cities.

However, compared to EUROCAT data our value is within the middle range.

The very high annual prevalences for cleft lip with or without cleft palate up to maximal 26.0 per 10,000 births registered in 1999 are again balanced in this way.

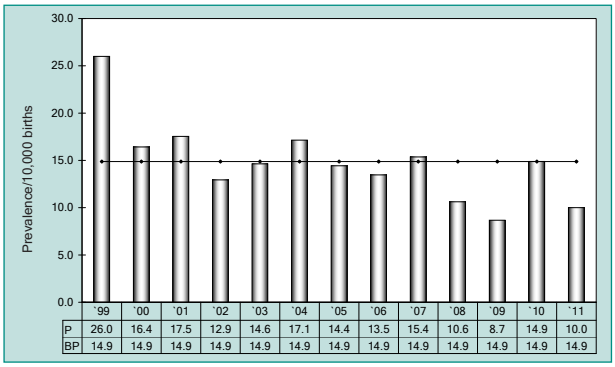
additiional information:

Pregnancy outcome	15 x live birth 1 x spontaneous abortion 1 x termination of pregnancy
Sex	10 x male 7 x female
Number of isolated malformations/MCA	6 x MCA 11 x isolated

Ten of the registered births were male and seven were female. In total 15 births were live births. One spontaneous abortion occured in combination with a severe chorioamnionitis after 18 weeks of gestation. In addition one termination of pregnacy was induced also afer 18 weeks of gestation as the foetus suffered from a Patau syndrome. We received information about the prenatal utrasound screening results in five of the registered cases.

Malformation combinations (MCA) or superordinated syndromes detected:

- Patau syndrome with: accessory 6th finger (postaxial) left, brachydactyly of finger bil., transverse palmar crease right, dysplastic, low set ears, wide nose bridge, thymus hypoplasia
- renal agenesis right
- multicystic dysplastic kidney left
- mitral valve insufficiency, sacral dimple
- combined sound conduction and perception disorder right (40 dB)
- sound conduction disorder bil.



	`99	`00	`01	`02	`03	`04	`05	`06	`07	`08	`09	`10	`11
P	26.0	16.4	17.5	12.9	14.6	17.1	14.4	13.5	15.4	10.6	8.7	14.9	10.0
BP	14.9	14.9	14.9	14.9	14.9	14.9	14.9	14.9	14.9	14.9	14.9	14.9	14.9

Fig. 21: Development of prevalence/10,000 births with cleft lip with or without cleft palate in the registration area since 1999

In 2011 one child with cleft lip with or without cleft palate per 999 births was registered in Saxony-Anhalt.

12.15 Cleft Palate (Q35.1/Q35.3/Q35.5/Q35.9)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle 2 x Magdeburg	3	6,3	↔
Districts: 1 x Anhalt-Bitterfeld 2 x Harz 2 x Salzlandkreis	5	4,1	↓
Saxony-Anhalt	**8**	**4,7**	↓

Cleft Palate (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	7,49	5,30 - 10,28
Districts	8,00	6,74 - 9,48
Region	7,88	6,78 - 9,14
EUROCAT	5,80	3,21 S Portugal* 13,66 Malta**

*/** centres with lowest resp. highest prevalence/10,000 births

The number of cleft palates is with eight registered births similar to the number of births we registered in the previous year. In 2011 the **prevalence** of **4.7 per 10,000 births** shows compared to the previous years a significant descending trend.

The annual prevalence 2011 of Saxony-Anhalt is clearly under the confidence of interval of 1999-2010 but within the middle range in comparison to EUROCAT data.
Similar to the congenital malformation cleft lip with or without cleft palate, the annual prevalences of 1995-2001 of cleft palate were very high by international comparison. These values are now balanced.

additiional information:

Pregnancy outcome	6 x live birth 2 x termination of pregnancy
Sex	1 x male 7 x female
Number of isolated malformations/MCA	3 x MCA 5 x isolated

The sex ratio shows a clear gynaecotrophism as mainly female infants were concerned.

When analysing the pregnancy outcome we registered six live births and two terminations of pregnancy after 19 and 20 weeks of gestation due the presence of a superordinated Down's syndrome and a VATER association.

Cleft palate occurred in five cases as isolated malformation.

Malformation combinations (MCA) or superordinated syndromes detected:

- Down's syndrome (mosaic trisomy) with: epicanthus internus bil., lateral ascending eyelids blt., low set ears, saddleback nose, mandibular micrognathia and retrognathia, brachydactyly of finger II bil.
- VACTERL association with: renal agenesis right, occipital encephalocele, cleft hand left, cloobhand with missing thumb and radius right, hypoplastic ulna right, hypoplastic gall bladder, missing cervical vertebra, multiple hemivertebra, butterfly vertebra and fusion of hemivertebra, missing ribs bilateral, hypoplastic aorta, malformation of the right upper eyelid, low-set right ear
- sound conduction disorder bil. (right 70 dB, left 60 dB)

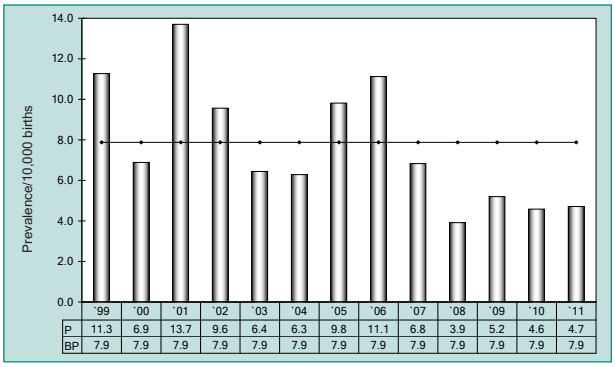


Fig. 22: Development of prevalence/10,000 births with cleft palate in the registration area since 1999

In 2011 one child with cleft palate per 2124 births was registered in Saxony-Anhalt.

12.16 Choanal Atresia (Q30.0)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities	0	0,0	↘
Districts: 1 x Salzlandkreis	1	0,8	↔
Saxony-Anhalt	**1**	**0,6**	↔

Choanal Atresia (1999-2010)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	0,59	0,12 - 1,73
Districts	0,45	0,18 - 0,93
Region	0,49	0,23 - 0,89
EUROCAT	0,87	0,10 S Portugal* 2,37 Mainz (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

One case of choanalatresia, which is a very rare appearing malformation was registered in 2011. The **prevalence** of **0.6 per 10,000 births** is within the confidence interval.

The frequency of appearrence of this malformation in Saxony-Anhalt is to be classified as rather low.

additiional information:

Pregnancy outcome	1 x live birth
Sex	1 x male
Number of isolated malformations/MCA	1 x isolated

This malformation of the choanae occured isolated in one male infant.

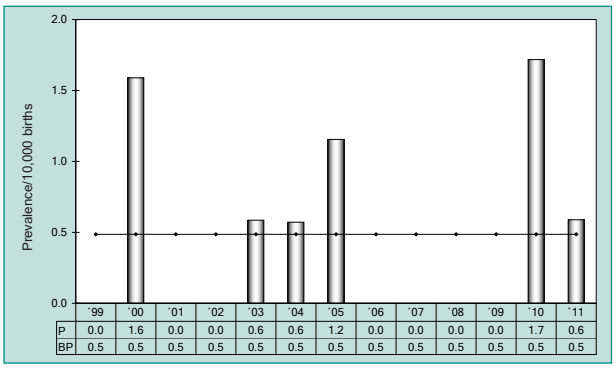


Fig. 23: Development of prevalence/10,000 births with choanal atresia in the registration area since 1999

In 2011 one child with a choanal atresia was registered per 16,989 births in Saxony-Anhalt.

12.17 Oesophageal Atresia/-Stenosis/-Fistula (Q39.0-Q39.4)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Magdeburg	1	2,1	↘
Districts: 1 x Anhalt-Bitterfeld 1 x Börde 1 x Harz	3	2,5	↔
Saxony-Anhalt	**4**	**2,4**	↔

Oesophageal Atresia/-Stenosis/-Fistula (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	3,75	2,26 - 5,85
Districts	2,32	1,63 - 3,22
Region	2,67	2,02 - 3,48
EUROCAT (Q39.0-Q39.1)	2,34	0,80 SE Ireland* 4,21 Strasbourg (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

Four births with oesosophageal atresia were registered in 2011. The corresponding **prevalence** of **2.4 per 10,000 births** remained unchanged in comparison to the previous yeras.

EUROCAT calculated a basic prevalence of 2.34 per 10,000 births for the years 1999-2010. The annual prevalence of Saxony-Anhalt is within this calculated range.

additiional information:

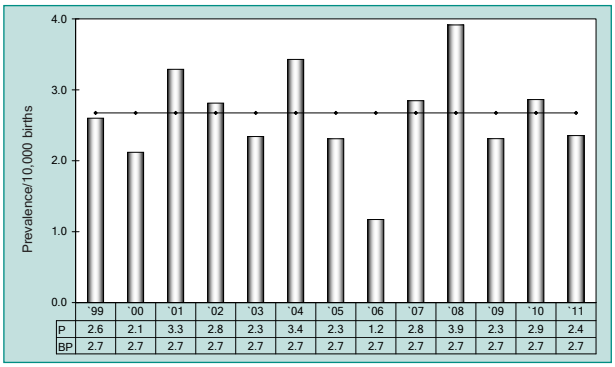
Pregnancy outcome	3 x live birth 1 x Stillbirth
Sex	2 x male 2 x female
Number of isolated malformations/MCA	4 x MCA

One infant was stillborn after 36 weeks of gestation. This hypotroph female infant suffered from an Edwards syndrome. During prenatal ultrasound screening oesophageal atresia, VDS and polyhydramnion were already confirmed.
Another three children with oesophageal atresia were delivered alive but hypotroph after 26 and 38 weeks of gestation. In three cases an oesophagotracheal fistula occured.

All births suffered from combined malformations or superordinated syndromes.

Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: VSD, malposition of hands, cerebellar anomaly
- trachea stenosis, tracheomalacia, ASD, hernia inguinalis left
- malformation of great arteries
- PFO and haemodynamic not effective PDA at full term infant



	`99	`00	`01	`02	`03	`04	`05	`06	`07	`08	`09	`10	`11
P	2.6	2.1	3.3	2.8	2.3	3.4	2.3	1.2	2.8	3.9	2.3	2.9	2.4
BP	2.7	2.7	2.7	2.7	2.7	2.7	2.7	2.7	2.7	2.7	2.7	2.7	2.7

Fig. 24: Development of prevalence/10,000 births with oesophageal atresia/stenosis/fistula in the registration area since 1999

In 2011 one oesophageal atresia/fistula per 4247 births was registered in Saxony-Anhalt.

12.18 Small Intestinal Atresia/Stenosis (Q41.1/Q41.2/Q41.8/Q41.9)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Magdeburg	1	2,1	↔
Districts: 1 x Salzlandkreis	1	0,8	↓
Saxony-Anhalt	**2**	**1,2**	↘

Dünndarmatresie/-stenose (1999-2010)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	1,38	0,55 - 2,84
Districts	2,13	1,47 - 2,99
Region	1,95	1,39 - 2,65
EUROCAT (Q41.1-Q41.8)	0,77	0,25 Wielkopolska (Poland)* 1,95 Isle de la Reunion (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

Two life births with small intestinal atresia were registered in 2011. Therefore, the **prevalence** of **1.2 per 10,000 births** is slighly under the basic prevalence of 1999-2010.

Compared with the European data of EUROCAT our prevalence 2011 is within the middle range.

additiional information:

Pregnancy outcome	2 x live birth
Sex	1 x male 1 x female
Number of isolated malformations/MCA	2 x MCA

In one infant the small intestinal atresia occurred in combination with a gastrochisis. This was already confirmed during prenatal ultrasound screening. On the contrary, the other small intestinal atresia was detected only postnatally.

Malformation combinations (MCA) or superordinated syndromes detected:

- microcephaly, PFO and haemodynamic not relevant PDA at preterm infant
- gastroschisis, PDA at preterm infant

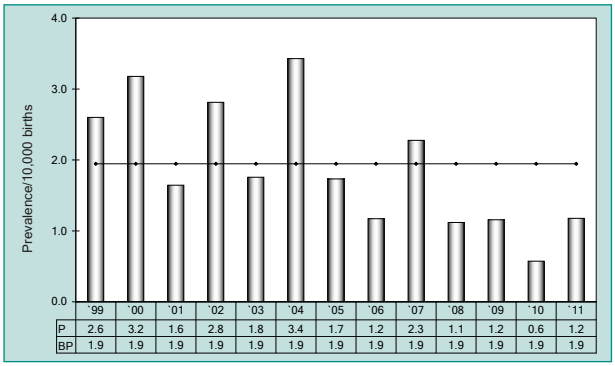


Fig. 25: Development of prevalence/10.000 births with small intestinal atresia/stenosis in the registration area since 1999

In 2011 one small intestinal atresia/stenosis per 8495 births was registered in Saxony-Anhalt.

12.19 Anorectal Atresia/Stenosis (Q42.0-Q42.3)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle 1 x Magdeburg	2	4,2	↔
Districts: 1 x Anhalt-Bitterfeld 1 x Harz 1 x Jerichower Land 2 x Saalekreis 2 x Stendal	7	5,7	↔
Saxony-Anhalt	**9**	**5,3**	↔

Anorectal Atresia/Stenosis (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	5,72	3,83 - 8,21
Districts	5,04	3,98 - 6,28
Region	5,20	4,33 - 6,24
EUROCAT	3,00	1,41 Zagreb (Croatia)* 6,72 Styria (Austria)**

*/** centres with lowest resp. highest prevalence/10,000 births

Since 2005 the frequency of appearance of anorectal atresia/stenosis is very high. The value of 2011 is within the basic prevalence, but during the whole registration period we observed an increasing trend of appearance (see also chapter 12.37). In 2011 nine births with anorectal atresia/stenosis were registered. This corresponds to a prevalence of 5.3 per 10,000 births and continues to be within the upper third in comparison to European data.

Also our calculated basic prevalence of 5.2 per 10,000 births for 1999-2010 is higher than the value calculated by EUROCAT. They determined a basic prevalence of 3.0 per 10,000 births for the same time period.

additiional information:

Pregnancy outcome	7 x live birth 2 x termination of pregnancy
Sex	4 x male 5 x female
Number of isolated malformations/MCA	5 x MCA 4 x isolated

The sex ratio is nearly balanced.

When considering the pregnancy outcome it shows that three-fourths of concerned infants were live births. In two cases a termination of pregnancy took place after 15 and 22 weeks of gestations. Both foetuses suffered from a Potter sequence and consequently additional malformations.

Only in four infants anorectal atresia/stenosis occurred isolated.

Malformation combinations (MCA) or superordinated syndromes detected:

- Potter sequence (functionless, hypoplastic kidney), club foot, malformation of heart and liver, hypoplastic lung bil.
- multicystic dysplastic kidney, pulmonary valve atresia, malformation of heart septum, hypoplastic gallbladder, missing pulmonary lobe right
- atresia of bile duct, Cat-eye-syndrome, coloboma of iris, sound conduction and perception disorder bil.. (right 60 dB, left 55 dB), pre-auricular appendix bil.
- PFO at full term infant, retarded hip left
- ASD

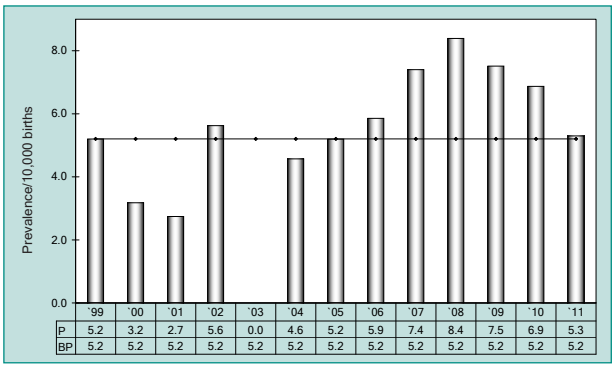


Fig. 26: Development of prevalence/10,000 births with anorectal atresia/-stenosis in the registration area since 1999

In 2011 one anorectal atresia/ stenosis per 1888 births was registered in Saxony-Anhalt.

12.20 Undescended Testis (Q53.1-Q53.9)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 2 x Magdeburg	2	4,2	↓
Districts: 1 x Anhalt-Bitterfeld 1 x Harz 1 x Saalekreis 1 x Wittenberg	4	3,3	↓
Saxony-Anhalt	**6**	**3,5**	↓

Undescended Testis (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	15,57	12,33 - 19,40
Districts	5,55	4,44 - 6,86
Region	8,02	6,91 - 9,30
EUROCAT	no informationn	no informationn

Six boys with undescended testis were registred in 2011. Generally, only full term infants are regarded in our analysis. As in the previous years, we received fewer reports about these malformations and therefore we have to assume that the congenital undescended testis is not reported in all cases.
The current prevalence of 3.5 per 10,000 births is therefore similar to the value of the previous year. However, in regard to the basic prevalence 1999-2010 our value is lower.

No EUROCAT data for comparison is present for undescended testis

additiional information:

Pregnancy outcome	6 x live birth
Sex	6 x male
2Number of isolated malformations/MCA	2 x MCA 4 x isolated

In one case the undescended testis occured in combination with diaphragmatic hernia.

Malformation combinations (MCA) or superordinated syndromes detected:

- diaphragmatic hernia left, syndactyly type I (III. / IV. finger) right
- volvulus

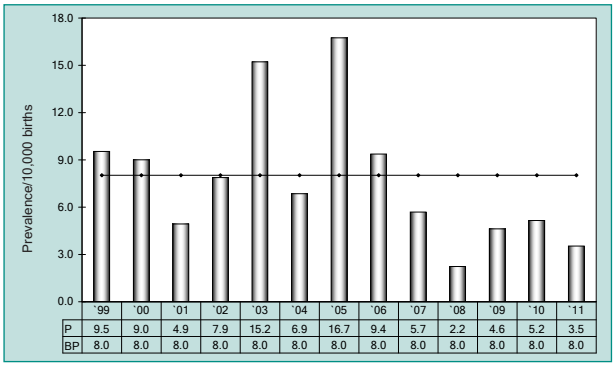


Fig. 27: Development of prevalence/10,000 births with undescended testis in the registration area since 1999

In 2011 one child with undescended testis per 2832 births (1456 boys) was registered in Saxony-Anhalt.

12.21 Hypospadias (Q54.0-Q54.3/Q54.8/Q54.9)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 2 x Dessau-Roßlau 4 x Halle 1 x Magdeburg	7	14,6	↓
Districts: 1 x Altmarkkreis Salzwedel 3 x Anhalt-Bitterfeld 3 x Burgenlandkreis 1 x Börde 4 x Harz 2 x Jerichower Land 3 x Saalekreis 3 x Salzlandkreis 1 x Stendal	21	17,2	↔
Saxony-Anhalt	**28**	**16,5**	↘

Hypospadias (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	20,30	16,83 - 24,44
Districts	18,46	16,48 - 20,67
Region	18,92	17,16 - 20,85
EUROCAT	16,76	3,61 NorthernEngland (UK)* 38,06 Malta**

*/** centres with lowest resp. highest prevalence/10,000 births

We registered 28 boys with hypospadias in 2011. Glandular, penile, scrotal and perineal hypospadias are included in our analysis by definition. The **prevalence** of **16.5 per 10,000 births** shows altogether a slightly decreasing trend in regard to the basic prevalence. When analysing data from the districts separately, the annual prevalence of 17.2 per 10,000 births is within the range of the previous years.

The prevalence of Saxony-Anhalt is within the middle range in comparison to EUROCAT data.

additiional information:

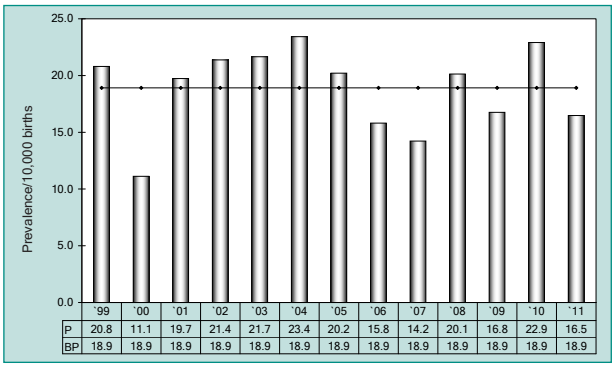
Pregnancy outcome	27 x live birth 1 x live birth descended after 7 days of life
Sex	28 x male
Number of isolated malformations/MCA	7 x MCA 21 x isolated

All infants were life births. One birth which deceased postnatal was a preterm infant of only 23 weeks of gestation.

In 43% of all cases the hypospadias occured glandular, 17% suffered from a penile hypospadias and 7% from a scrotal hypospadias. We received no further specifications in 33% of the cases

Malformation combinations (MCA) or superordinated syndromes detected:

- 2 x haemodynamical relevant PDA at preterm infant
- ASD II, lateral penile deviation
- 2 x lateral penile deviation
- DUP II. grade bil.
- acsessory 6th finger right, retarded hip bil.



	`99	`00	`01	`02	`03	`04	`05	`06	`07	`08	`09	`10	`11
P	20.8	11.1	19.7	21.4	21.7	23.4	20.2	15.8	14.2	20.1	16.8	22.9	16.5
BP	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9

Fig. 28: Development of prevalence/10,000 births with hypospadias in the registration area since 1999

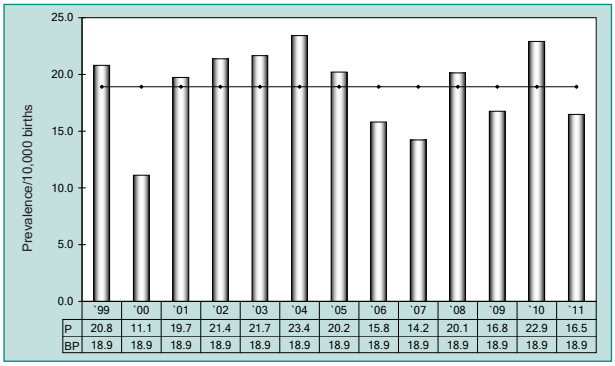
In 2011 one hypospadias per 607 births (312 boys) was registered in Saxony-Anhalt.

12.22 Epispadias (Q64.0)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities	0	0,0	↔
Districts	0	0,0	↓
Saxony-Anhalt	0	0,0	↓

Epispadias (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	0,20	0,00 - 1,10
Districts	0,45	0,18 - 0,93
Region	0,39	0,17 - 0,77
EUROCAT	no informationn	no informationn

In 2011 no case of epispadias was registered.
The basic prevalence of 1999-2010 is at 0.39 per 10,000 births



	`99	`00	`01	`02	`03	`04	`05	`06	`07	`08	`09	`10	`11
P	20.8	11.1	19.7	21.4	21.7	23.4	20.2	15.8	14.2	20.1	16.8	22.9	16.5
BP	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9

Fig. 29: Development of prevalence/10,000 births with epispadias in the registration area since 1999

In 2011 no birth with epispadias was registered in Saxony-Anhalt.

12.23 Indeterminate Sex (Q56.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities	0	0,0	↔
Districts	0	0,0	↓
Saxony-Anhalt	0	0,0	↓

Indeterminate Sex (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	0,20	0,00 - 1,10
Districts	0,77	0,40 - 1,35
Region	0,63	0,34 - 1,08
EUROCAT	0,67	0,30 Basque Country (Spain)* 1,87 SE Ireland**

*/** centres with lowest resp. highest prevalence/10,000 births

In 2011 no births with indeterminate sex was registered. The basic prevalence of the registration period 1999-2010 is at 0.63 per 10,000 births

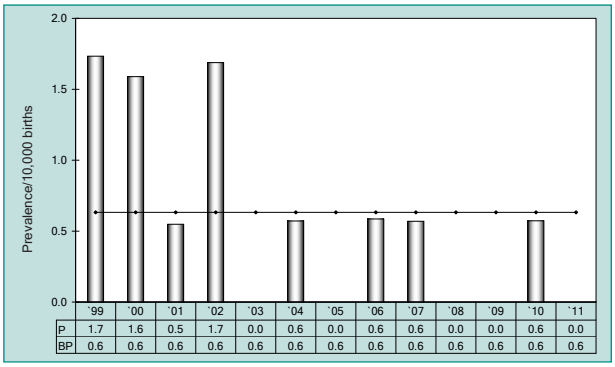


Fig. 30: Development of prevalence/10,000 births with indeterminate sex in the registration area since 1999

In 2011 no birth with indeterminate sex was registered in Saxony-Anhalt.

12.24 Potter Sequence (Q60.6)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 2 x Magdeburg	2	4,2	↑
Districts: 1 x Jerichower Land 1 x Saalekreis	2	1,6	↔
Saxony-Anhalt	**4**	**2,4**	↔

Potter Sequence (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	1,38	0,55 - 2,84
Districts	2,19	1,52 - 3,07
Region	1,99	1,43 - 2,70
EUROCAT	1,24	0,58 Hungary* 5,00 Mainz (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

We registered four births with Potter sequence in 2011. The prevalence of 2.4 per 10,000 births is therefore within the confidence interval of the registration period 1999-2010.

Compared to other European malformation registration centres, the annual prevalence of Saxony-Anhalt is slightly above the basic prevalence which was calculated by EUROCAT. The highest basic prevalence of 5.0 per 10,000 births was registered in Mainz

additiional information:

Pregnancy outcome	1 x live birth descended within 7 days of life 2 x termination of pregnancy 1 x stillbirth
Sex	2 x male 1 x female 1 x no information
Number of isolated malformations/MCA	3 x MCA 1 x isolated

One infant with Potter sequence was born alive but descended after 7 days of life. One female infant was stillborn after 24 weeks of gestation. It suffered from Potter sequence with cardiomyopathy; this diagnosis was already confirmed prenatally. Furthermore, in two cases a termination of pregnancy was induced after 22 and 18 weeks of gestation.

Malformation combinations (MCA) or superordinated syndromes detected:

- holoprosencephaly, missing nasal septum, malformation of pharynx, shortened upper and lower lims bil.
- anal atresia, club foot, malformation of heart and liver, hypoplastic lung bil.
- ureter agenesia left, wide nasal root

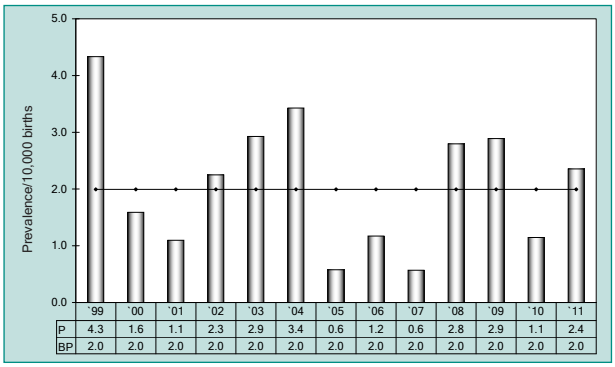


Fig. 31: Development of prevalence/10,000 births with Potter sequence in the registration area since 1999

In 2011 one Potter sequence per 4247 births was registered in Saxony-Anhalt.

Please note:

What is Sartan fetopathie?

The group of pharmaceuticals sartans were developed from ACE inhibitors. Mainly used in the antyhypertensive therapy, they have a teratogenic effect in case of maternal intake during second and third trimenon of pregnancy.
The suspected pathomechanism of both substances is a reduced perfusion of the foetal organs, in particular of the kidneys. That means both substances interrupt the renin-angiotensin system at different points. The result of such a foetal damage is an intrauterine oliguria. Since the amniotic fluid production depends from the second trimenon mainly from foetal urine production, an oligohydramnios can occur which might be diagnosed by prenatal ultrasound screening. This leads into **occurrence of a potter sequence** with lung and thorax hypoplasia, distorsion of limbs, characteristic face and further consequential problems. Concerned infants often suffer postnatal from a renal failure which is in most cases not reversible. Additionally, a hypoplasia/dysplasia of the cranial bone can occur at insufficient cranial ossification.
No secure data is present about an increased risk of fetopathie as a result of maternal intake of ACE inhibitors or sartans during first trimenon of pregnancy.

12.25 Renal Agenesis, Unilateral (Q60.0/Q60.2)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 2 x Dessau-Roßlau 3 x Halle 1 x Magdeburg	6	12,5	↑
Districts: 1 x Altmarkkreis Salzwedel 1 x Anhalt-Bitterfeld 1 x Jerichower Land 1 x Saalekreis 1 x Salzlandkreis 1 x Stendal	6	4,9	↓
Saxony-Anhalt	**12**	**7,1**	↔

Renal Agenesis, Unilateral (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	7,69	5,47 - 10,51
Districts	6,78	5,63 - 8,14
Region	7,00	5,97 - 8,20
EUROCAT	no informationn	no informationn

Twelve births with unilateral renal agenesis were registered in 2011.
The prevalence of 7.1 per 10,000 births is within the basic prevalence of 1999-2010.

No EUROCAT data is present for comparison.

additiional information:

Pregnancy outcome	10 x live birth 1 x termination of pregnancy 1 x stillbirth
Sex	6 x male 6 x female
Number of isolated malformations/MCA	5 x MCA 7 x isolated

One stillbirth after 37 weeks of gestation of a male hypotroph infant with renal agenesis was reported. The reason for this incident was a placental insufficiency. Furthermore, one pregnancy was terminated after 20 weeks of gestation due to occurrence of a VACTERL-association. The remaining ten infants were born alive.

Malformation combinations (MCA) or superordinated syndromes detected:

- VACTERL association with: cleft of hard palate, occipital encephalocele, cleft hand left, club hand with missing thumb and radius right, hypoplastic ulna right, hypoplastic gall bladder, missing cervical vertebra, multiple hemivertebra, butterfly vertebra and fusion of hemivertebra, missing ribs bilateral, hypoplastic aorta, malformation of the right upper eyelid, low-set right ear
- cleft lip with or without cleft palate
- hip subluxation
- ovarian cyst
- agenesis of ureter left

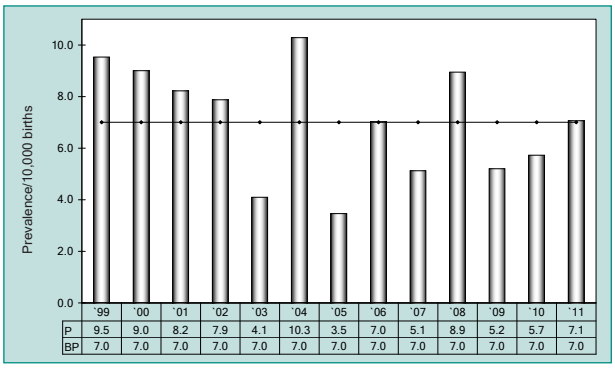


Fig. 32: Development of prevalence/10,000 births with unilateral renal agenesis in the registration area since 1999

In 2011 one renal agenesis, unilateral per 1416 births was registered in Saxony-Anhalt.

12.26 Cystic Kidney (Q61.1-Q61.9)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 3 x Halle 3 x Magdeburg	6	12,5	↔
Districts: 2 x Anhalt-Bitterfeld 1 x Burgenlandkreis 2 x Börde 1 x Harz 1 x Mansfeld-Südharz 3 x Saalekreis	10	8,2	↔
Saxony-Anhalt	**16**	**9,4**	↔

Cystic Kidney (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	9,66	7,15 - 12,77
Districts	8,13	6,86 - 9,62
Region	8,51	7,36 - 9,82
EUROCAT	no informationn	no informationn

*/** centres with lowest resp. highest prevalence/10,000 births

The registered number of 16 births with cystic kidneys remains unchanged in comparison to the previous years. We calculated a **prevalence** of **9.4 per 10,000 births**. This prevalence is within the confidence interval, in the major cities as well as in the districts.

EUROCAT does not publish any data regarding this congenital malformation in which are poly as well as multycystic renal diseases are summarised

additiional information:

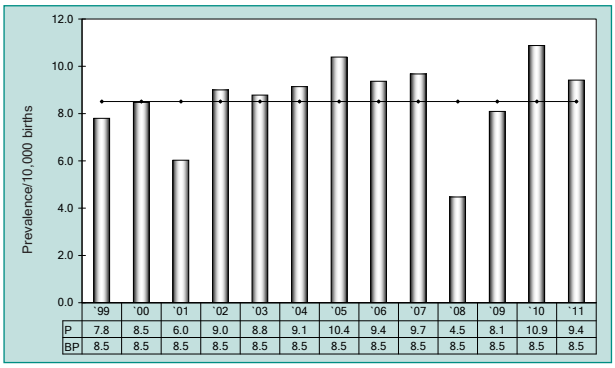
Pregnancy outcome	14 x live birth 2 x termination of pregnancy
Sex	12 x male 4 x female
Number of isolated malformations/MCA	9 x MCA 7 x isolated

The sex ratio shows a clear androtrophism since twelve male and only four female infants were concerned.

14 infants were born alive. In eleven cases the diagnosis of cystic kidney or a similar disease was already confirmed prenatally. Two pregnancies were terminated after 15 and 22 weeks of gestation. One infant suffered from additional severe malformations like rectal atresia, pulmonary valve atresia, hpoplastic gall bladder and a missing right lung lobe.

Malformation combinations (MCA) or superordinated syndromes detected:

- rectal atresia, pulmonary valve atresia, hypoplastic gall baldder, missing right lung lobe
- cleft of hard palate with cleft palate
- Caroli syndrome with: choledochus cyst, polycystic liver, hepatomegaly, craniofacial dysmorphy
- VSD
- ASD
- urethral stenosis left
- urethral valves in the back of urethra
- DUP IV. grade right
- accessory 6th toe right, retarded hip bil.



	'99	'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11
P	7.8	8.5	6.0	9.0	8.8	9.1	10.4	9.4	9.7	4.5	8.1	10.9	9.4
BP	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5

Fig. 33: Development of prevalence/10,000 births with cystic kidneys in the registration area since 1999

In 2011 one cystic kidney per 1062 births was registered in Saxony-Anhalt.

12.27 Bladder Exstrophy (Q64.1)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities	0	0,0	↔
Districts	0	0,0	↘
Saxony-Anhalt	0	0,0	↘

Bladder Exstrophy (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	0,00	0,00 - 0,59
Districts	0,19	0,04 - 0,57
Region	0,15	0,03 - 0,43
EUROCAT	no informationn	no informationn

No birth with the rarely occurring malformation bladder exstrophy was registered in 2011.
The basic prevalence is at 0.15 per 10,000 births for the registration period 1999-2010

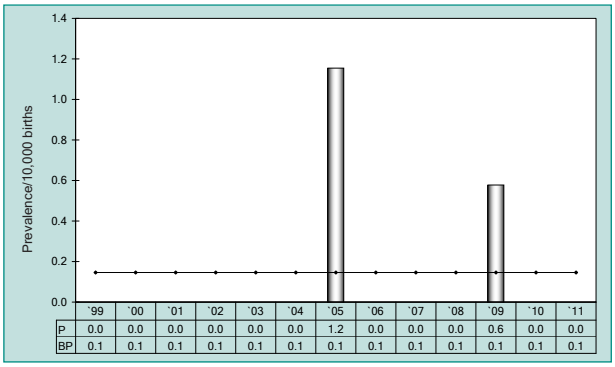


Fig. 34: Development of prevalence/10,000 births with bladder exstropy in the registration area since 1999

In 2011 no birth with a bladder exstrophy was registered in Saxony-Anhalt.

12.28 Preaxial Polydactyly (Q69.1/Q69.2)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Dessau-Roßlau	1	2,1	↓
Districts: 1 x Anhalt-Bitterfeld 1 x Burgenlandkreis 1 x Börde 1 x Harz 1 x Stendal	5	4,1	↔
Saxony-Anhalt	**6**	**3,5**	↘

Preaxial Polydactyly (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	4,93	3,19 - 7,27
Districts	4,26	3,30 - 5,42
Region	4,43	3,56 - 5,43
EUROCAT	no informationn	no informationn

In 2011 six infants with preaxial polydactyly were born in Saxony-Anhalt.
The **prevalence** of **3.5 per 10,000 births** is slightly lower than the basic prevalence. We registered only one child with this malformation from the major cities.

Comparative EUROCAT data for preaxial polydactyly is not available

additiional information:

Pregnancy outcome	6 x live birth
Sex	5 x male 1 x female
Number of isolated malformations/MCA	3 x MCA 3 x isolated

The sex ratio shows a clear androtropism.

The preaxial polydactyly occurred in three cases isolated and in three cases in combination with additional malformations of hands and feet, resp. in one case with PFO.
Two births had a positive family history in regard to congenital malformations. One mother also suffered from a preaxial polydactyly.

Malformation combinations (MCA) or superordinated syndromes detected:

- accessory 6th finger with osseous parts bil., one additional accessory toe left
- crossed polysyndactyly with: membranous syndactyly of toes 1/2/3 right and 1/2 left, accessory 6th finger bil.
- PFO at full term infant

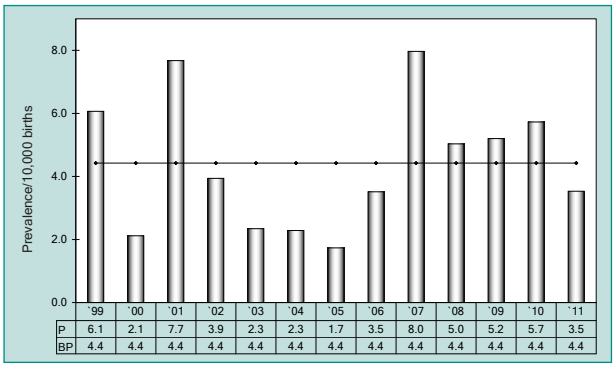


Fig. 35: Development of prevalence/10,000 births with preaxial polydactyly in the registration area since 1999

In 2011 one preaxial polydactyly per 2832 births was registered in Saxony-Anhalt.

12.29 Limb Reduction Defects of both Upper and Lower Limbs (Q71./Q72./Q73.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 4 x Halle 2 x Magdeburg	6	12,5	↑
Districts: 1 x Anhalt-Bitterfeld 1 x Burgenlandkreis 3 x Mansfeld-Südharz 1 x Saalekreis 1 x Stendal	7	5,7	↓
Saxony-Anhalt	**13**	**7,7**	↔

Limb Reduction Defects, in total (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	7,49	5,30 - 10,28
Districts	8,00	6,74 - 9,48
Region	7,88	6,78 - 9,14
EUROCAT	5,59	2,01 SE Ireland* 12,10 Mainz (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

We registered 13 births with reductions defects of upper and lower limbs.
The **prevalence** of **7.7 per 10,000 births** is higher than the prevalence we calculated in 2010 and 2009 but it is in regard to the basic prevalence within the middle range.

When comparing the prevalences from Saxony-Anhalt with European data, our values are higher than the calculated basic prevalences. We outlined this information already in our previous annual reports. However, the transmitted data from our colleagues in Mainz are still clearly higher.

additiional information:

Pregnancy outcome	9 x live birth 1 x live birth descended within 7 days of life 3 x termination of pregnancy
Sex	5 x male 8 x female
Number of isolated malformations/MCA	8 x MCA 5 x isolated

Ten infants were born alive, they suffered from mainly mild forms of limb reduction defects. One infant was delivered after 34 weeks of gestation, unfortunately it deceased postnatal. In this case a body stalk anomaly was already confirmed during prenatal ultrasound screening. Terminations of pregnancy took place after 16, 17 and 20 weeks of gestation. Amongst others an Edward syndrome and VACTERL-Association were diagnosed prenatally in these cases.

In more than 60% of the registered cases the limb reduction defects occurred in combination with other malformations or superordinated syndromes.

Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: omphalocele, club foot, dislodged wrist, right, incompletely lobed lung right, mesenterium ileocolicum commune, intestinal malrotation, hypoplastic pancreas, spleen asplenia, VSD, renal hypoplasia left, thymus hypoplasia
- VACTERL association with: cleft of the hard palate, occipital encephalocele, renal agenesis right, hypoplastic gall bladder, missing cervical vertebra, multiple hemivertebra, butterfly vertebra and fusion of hemivertebra, missing ribs bilateral, hypoplastic aorta, malformation of the right upper eyelid, low-set right ear
- body stalks anomaly with: intestinal malrotation, missing left half of diaphragm, deformation of vertebral column, membranous syndactyly type I (II. / III. toe) right, transverse palmar crease left, cleft uvula, low set ears
- missing diaphragm and pelvis left with prolapse of abdominal organs, hypoplasia of osseous thorax, of lung blt. and of heart, nuchal oedema, dysplastic low set ears
- anotia right, amniotic band sequence at right hand and at both feet, overlapping toes blt., transverse palmar crease left
- amniotic band sequence at left hand
- 2 x osseous syndactyly of fingers (1 x blt., 1 x left)

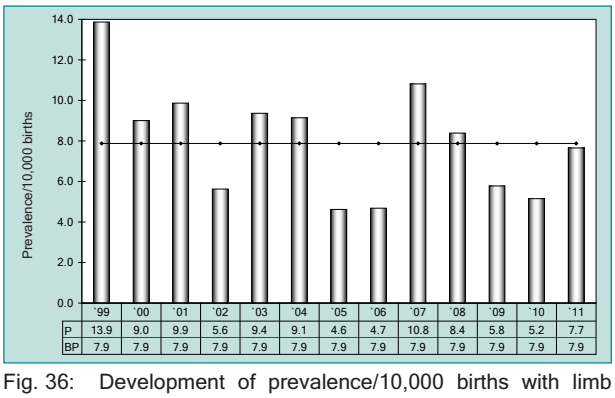


Fig. 36: Development of prevalence/10,000 births with limb reduction defects in the registration area since 1999

In 2011 one limb reduction defect per 1307 births was registered in Saxony-Anhalt.

12.30 Diaphragmatic Hernia (Q79.0/Q79.1)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle 1 x Magdeburg	2	4,2	↔
Districts: 1 x Wittenberg	1	0,8	↓
Saxony-Anhalt	**3**	**1,8**	↓

Diaphragmatic Hernia (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	4,73	3,03 - 7,04
Districts	2,26	1,57 - 3,14
Region	2,87	2,18 - 3,70
EUROCAT (Q79.0)	2,70	0,88 S Portugal* 4,55 Strasbourg (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

Three births with diaphragmatic hernia were registered in 2011. The prevalence of diaphragmatic hernia in Saxony-Anhalt is at 1.8 per 10,000 births and therefore clearly under the basic prevalence and outside the confidence interval. We registered similar data in 2001 and 2005.

In comparison with data from other EUROCAT centres, our values is lower than the middle range.

additiional information:

Pregnancy outcome	1 x live birth 1 x live birth descended within 7 days of life 1 x termination of pregnancy
Sex	2 x male 1 x female
Number of isolated malformations/MCA	3 x MCA

In one male eutrophic live born case of 40th weeks of gestation the malformation was not diagnosed prenatally.

One infant was born alive after 34 weeks of gestation but descended postnatal. In addition to the diaphragmatic hernia a body stalk anomaly was confirmed during prenatal ultrasound screening. One infant suffered additionally from reduction defects of the lower limbs, pelvis, malformations of thorax, heart, lung and abdominal organs. Therefore, the pregnancy was terminated after 17 weeks of gestations.

Malformation combinations (MCA) or superordinated syndromes detected:

- body stalk anomaly with: intestinal malrotation, cleft foot left, longitudinal reduction defect of radius and ulna left, missing thumb left, deformation of vertebral column, membraneous syndactyly type I (II. / III. toe) right, transverse palmar crease left, cleft uvula, low set ears
- phokomelia of leg and missing big toe left, missing left pelvis with prolapse of abdominal organs, hypoplasia of osseous thorax, lung blt. and heart, nuchal oedema, dysplastic low set ears
- undescended testis left, syndactyly type I (III. / IV. finger) right

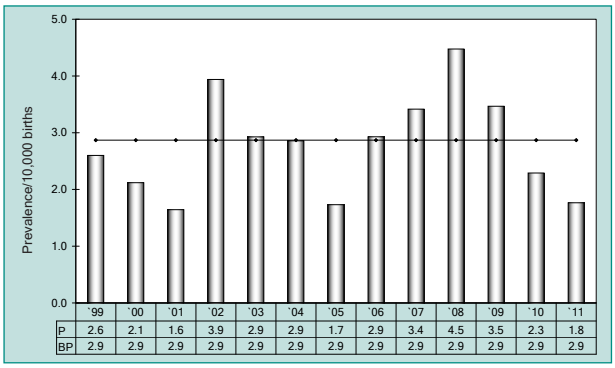


Fig. 37: Development of prevalence/10,000 births with diaphragmatic hernia in the registration area since 1999

In 2011 one diaphragmatic hernia per 5663 births was registered in Saxony-Anhalt.

12.31 Omphalocele (Q79.2)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle 1 x Magdeburg	2	4,2	↔
Districts: 2 x Mansfeld-Südharz 2 x Saalekreis	4	3,3	↔
Saxony-Anhalt	**6**	**3,5**	↔

Omphalocele (1999-2010)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	2,56	1,36 - 4,38
Districts	3,36	2,51 - 4,40
Region	3,16	2,44 - 4,03
EUROCAT	2,85	0,54 S Portugal* 5,66 Paris (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

The prevalence analysis of omphalocele shows an unchanged trend also in this year. In total, six births with this malformations were registered. The **prevalence** of **3.5 per 10,000 births** is within the confidence interval of the registration period 1999-2010.

In comparison with EUROCAT data the prevalences of the major cities and districts of Saxony-Anhalt are slightly above the middle range.

additiional information:

Pregnancy outcome	3 x live birth 3 x termination of pregnancy
Sex	5 x male 1 x female
Number of isolated malformations/MCA	3 x MCA 3 x isolated

The sex ratio shows an androtropism.

The pregnancy outcome shows that 50% were live births. In two cases the diagnosis omphalocele was confirmed prenatally. Also in 50% of the cases a termination of pregnancy took place between 14 and 19 weeks of gestation. One infant suffered additionally from a canalis atrioventricularis communis and another suffered from an Edwards syndrome.

Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: missing radius and hypoplastic thumb right, club foot, dislodged wrist right, incompletely lobed lung right, mesenterium ileocolicum commune, intestinal malrotation, hypoplastic pancreas, spleen alplenia, VSD, renal hypoplasia left, thymus hypoplasia
- canalis atrioventricularis communis
- intestinal malrotation

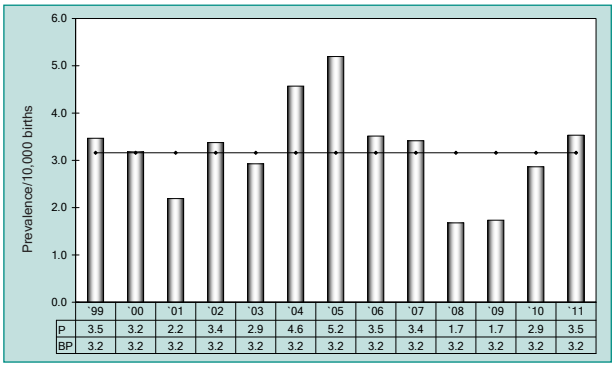


Fig. 38: Development of prevalence/10,000 births with omphalocele in the registration area since 1999

In 2011 one omphalocele per 2832 births was registered in Saxony-Anhalt.

12.32 Gastroschisis (Q79.3)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle 2 x Magdeburg	3	6,3	↔
Districts: 2 x Anhalt-Bitterfeld 1 x Jerichower Land 1 x Mansfeld-Südharz 1 x Salzlandkreis	5	4,1	↔
Saxony-Anhalt	**8**	**4,7**	↔

Gastroschisis (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	4,34	2,72 - 6,56
Districts	3,62	2,73 - 4,69
Region	3,79	3,00 - 4,73
EUROCAT	2,51	0,81 Tuscany (Italy)* 6,58 Mainz (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

The prevalence of gastrochisis is just as in the previous years with eight registered births on a high level. At the same time the value is within the confidence interval of the years 1999-2010.
The **prevalence** of **4.7 per 10,000 births** in Saxony-Anhalt is still in the upper range of the European basic prevalence.

additiional information:

Pregnancy outcome	6 x live birth 1 x termination of pregnancy 1 x stillbirth
Sex	3 x male 4 x female 1 x no information
Number of isolated malformations/MCA	4 x MCA 4 x isolated

In case of six life births the diagnosis gastrochisis was already confirmed prenatally. They were delivered between 32 and 33 weeks of gestation in a centre of perinatal care by elective caesarean section.
One female foetus with gastrochisis was stillborn after 37 weeks of gestation.
In one case the prenatal diagnosis of gastrochisis led to a termination of pregnancy after 14 weeks of gestation.

Malformation combinations (MCA) or superordinated syndromes detected:

- atresia of jejunum, PDA at preterm infant
- Meckel's diverticulum, mesenterium ileocolicum commune, intestinal malrotation, PFO at preterm infant
- prolapse of large intestine and parts of small intestine, connection from mesocolon to frontside lateral abdonimal wall, microcolon, PFO at preterm infant
- ASD II, haeodynamic not relevant PDA at preterm infant

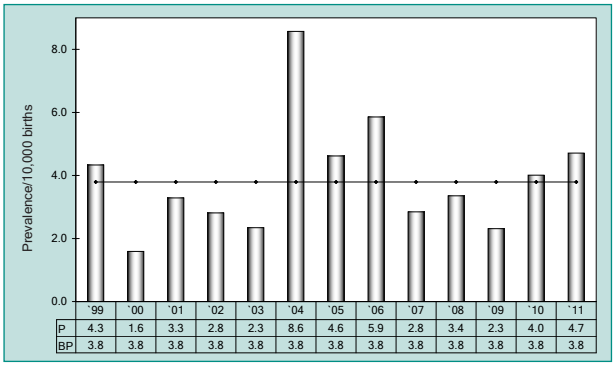


Fig. 39: Development of prevalence/10,000 births with gastroschisis in the registration area since 1999

In 2011 one gastroschisis per 2124 births was registered in Saxony-Anhalt.

12.33 Prune Belly Sequence (Q79.4)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 2 x Halle	2	4,2	↑
Districts: 1 x Mansfeld-Südharz 1 x Salzlandkreis	2	1,6	↑
Saxony-Anhalt	**4**	**2,4**	↑

Prune Belly Sequence (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	0,79	0,21 - 2,02
Districts	0,71	0,35 - 1,27
Region	0,73	0,41 - 1,20
EUROCAT	no informationn	no informationn

We registered four births with Prune belly syndrome in 2011.
The **prevalence** is therefore at **2.4 per 10,000 births** in Saxony-Anhalt.

A European comparison is not possible in this case, as no EUROCAT data are present for this malformation. Furthermore, scientific literature does not provide any valid data about a birth prevalence of Prune belly syndrome. Some review articles only provide a live birth prevalence of 1 : 35.000 up to 1 : 50.000. We calculated a higher annual prevalence, but our basic prevalence corresponds to these indications.

additiional information:

Pregnancy outcome	1 x live birth descended within 7 days of life 2 x termination of pregnancy 1 x stillbirth
Sex	4 x male
Number of isolated malformations/MCA	2 x MCA 2 x isolated

Depending from the severity of malformations Prune belly syndrome often has a lethal result. The above illustrated pregnancy outcome underlines this statement.
In one case the foetus of a 16 years old women was stillborn after 22 weeks of gestation. Malformations of kidneys and urinary system were detected already during prenatal ultrasound screening.
In two cases a termination of pregnancy was induced after 18 and 20 weeks of gestation.
A hypotroph preterm infant was born after 28 weeks of gestation but descended postnatal. In this case we have no information about prenatal findings.

Malformation combinations (MCA) or superordinated syndromes detected:

- hypoplastic lung bil., club foot, megacystis, hypertelorism
- urethral valves in the rear part of urethra, DUP

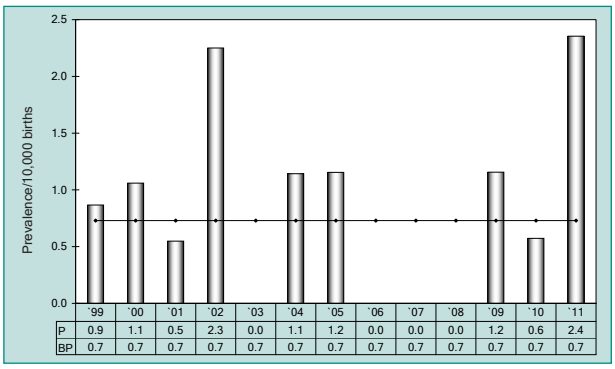


Fig. 40: Development of the prevalence/10,000 births with prune belly syndrome in the registration area since 1999

In 2011 one Prune belly syndrome per 4247 births was registered in Saxony-Anhalt.

12.34 Down Syndrome - Trisomy 21 (Q90.)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 2 x Dessau-Roßlau 6 x Halle 3 x Magdeburg	11	23,0	↔
Districts: 2 x Anhalt-Bitterfeld 1 x Burgenlandkreis 3 x Börde 4 x Harz 2 x Saalekreis 2 x Salzlandkreis 1 x Stendal 1 x Wittenberg	16	13,1	↘
Saxony-Anhalt	**27**	**15,9**	↔

Down Syndrome (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	20,50	17,01 - 24,65
Districts	15,56	13,75 - 17,59
Region	16,78	15,13 - 18,60
EUROCAT	20,01	7,79 S Portugal* 39,31 Paris (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

The Monitoring of Congenital Malformations registered 27 births with Down syndrome in Saxony-Anhalt in 2011. The current prevalence of 15.9 per 10,000 births is within the middle range of the basic prevalence and within the confidence interval of the registration period 1999-2010. The value we registered in the districts was slightly lower than expected.

EUROCAT calculated a basic prevalence of 20.01 per 10,000 births. In comparison to this prevalence, the data from Saxony-Anhalt is slightly lower in 2011

additiional information:

Pregnancy outcome	9 x live birth 18 x termination of pregnancy
Sex	10 x male 12 x female 5 x no information
9Number of isolated malformations/MCA	9 x MCA 18 x isolated

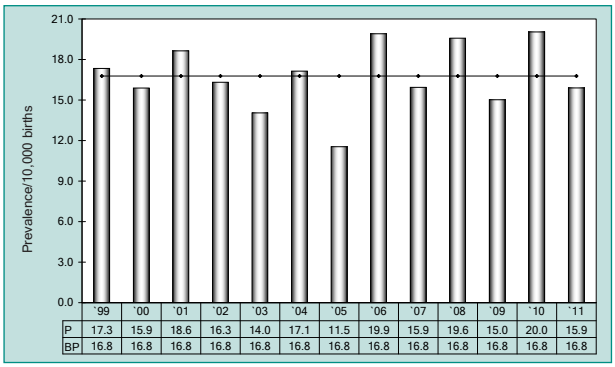
The sex ratio is balanced.

We registered 27 births with Down syndrome in 2011. As in the previous years only one third of the registered infants was born alive, the diagnosis was confirmed prenatally only in two cases. Four of the nine infants showed additional heart defects. We have no information about findings of invasive prenatal diagnostics in most cases. Two women aged 35 and 40 denied an amniocentesis.

In 18 cases we received only the diagnosis Down syndrome resp. information about presence of typical stigmata. Nine infants suffered from additional, mainly cardiac malformations.

Malformation combinations (MCA) or superordinated syndromes detected:

- microcephaly, DUP III. grade bil., megaureter left
- cleft of the soft palate
- canalis atrioventricularis communis, overriding aorta, mitral valve insufficiency, haemodynamic effective PDA at full term infant, tricuspidal insufficieny 1st grade
- ASD, PDA at full term infant
- canalis atrioventricularis communis, PFO at full term infant, anomaly of septum pellucidum
- canalis atrioventricularis communis
- atresia of duodenums, pancreas anulare, PFO at full term infant, hemangioma
- mesenterium ileocolicum commune
- epilepsy



	'99	'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11
P	17.3	15.9	18.6	16.3	14.0	17.1	11.5	19.9	15.9	19.6	15.0	20.0	15.9
BP	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8

Fig. 41: Development of prevalence/10,000 births with Down syndrome in the registration area since 1999

In 2011 one Down syndrome (trisomy 21) per 629 births was registered in Saxony-Anhalt.

12.35 Patau Syndrome - Trisomy 13 (Q91.4-Q91.7)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Magdeburg	1	2,1	↔
Districts: 1 x Börde	1	0,8	↔
Saxony-Anhalt	**2**	**1,2**	↔

Patau-Syndrome (1999-2010)		
	Basic prevalence /10,000 births	**Confidence Interval (CI of 95%) /10,000 births**
Cities	1,38	0,55 - 2,84
Districts	0,84	0,45 - 1,43
Region	0,97	0,59 - 1,50
EUROCAT	1,79	0,26 Zagreb (Croatia)* 3,92 Paris (France)**

*/** centres with lowest resp. highest prevalence/10,000 births

In 2011 two foetuses with trisomy 13 were registered. The current prevalence of 1.2 per 10,000 births is within the confidence interval of the previous years and remains stable.

Our data from Saxony-Anhalt is below the basic prevalence of EUROCAT.

additiional information:

Pregnancy outcome	2 x termination of pregnancy
Sex	1 x male 1 x female
Number of isolated malformations/MCA	1 x MCA 1 x isolated

The genetic examination showed in both cases the result of a meiotic nondisjunction.
In one case the amniocentesis took place for reasons of maternal age. A termination of pregnancy took place after a Patau syndrome was confirmed. In the other case specific softmarker were detected during prenatal ultrasound screening.

Malformation combinations (MCA) or superordinated syndromes detected:

- cleft lip with and with cleft palate blt. accessory 6th finger (postaxial) left, thymus hypoplasia

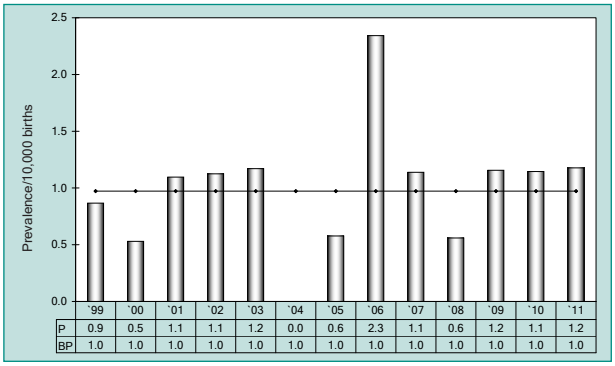


Fig. 42: Development of prevalence/10,000 births with a Patau syndrome in the registration area since 1999

In 2011 one Patau syndrome (trisomy 13) per 8495 births was registered in Saxony-Anhalt.

12.36 Edwards Syndrome - Trisomy 18 (Q91.0-Q91.3)

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities: 1 x Halle 1 x Magdeburg	2	4,2	↔
Districts: 1 x Altmarkkreis Salzwedel 1 x Burgenlandkreis 1 x Harz 1 x Mansfeld-Südharz	4	3,3	↔
Saxony-Anhalt	**6**	**3,5**	↔

Edwards-Syndrome (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	4,14	2,56 - 6,33
Districts	3,55	2,67 - 4,62
Region	3,70	2,91 - 4,63
EUROCAT	4,45	0,75 Ukraine* 8,68 Mainz (Germany)**

*/** centres with lowest resp. highest prevalence/10,000 births

We registered six births with Edwards syndrome in 2011. These are less cases than we registered in the previous three years.
The prevalence of 3.5 per 10,000 births is within the confidence interval of the registration period 1999-2010 and at the same time within the European middle range.

additiional information:

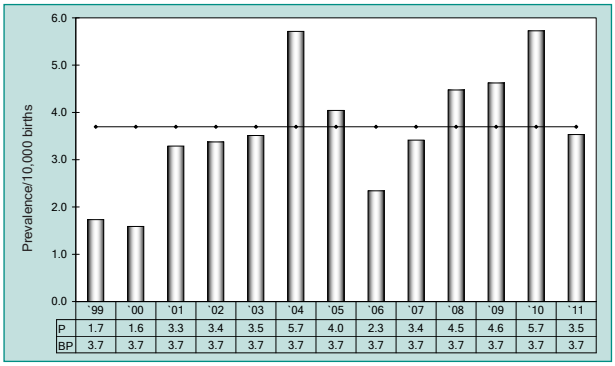
Pregnancy outcome	1 x live birth 4 x termination of pregnancy 1 x stillbirth
Sex	3 x male 3 x female
Number of isolated malformations/MCA	3 x MCA 3 x isolated

One hypotroph female preterm infant was stillborn after 36 weeks of gestation. It suffered in addition from complex internal malformations.

One infant was born alive after 40 weeks of gestation. It suffered additionally from a pentalogy of fallot. We have no information regarding prenatal diagnostics in this case. Two terminations of pregnancy took place after invasive prenatal diagnostics and confirmation of diagnosis. The reason to realise an amniocentesis was a maternal age of more than 35 years.

Malformation combinations (MCA) or superordinated syndromes detected:

- omphalocele, missing radius and hypoplastic thumb right, club foot, dislodged wrist right, incompletely lobed lung right, mesenterium ileocolicum commune, intestinal malrotation, hypoplastic pancreas, asplenia of spleen, VSD, renal hypoplasy left, thymus hypoplasia
- oesophageal atresia, VSD, malposition of hand, cerebellar anomaly
- pentalogy of fallot



	`99	`00	`01	`02	`03	`04	`05	`06	`07	`08	`09	`10	`11
P	1.7	1.6	3.3	3.4	3.5	5.7	4.0	2.3	3.4	4.5	4.6	5.7	3.5
BP	3.7	3.7	3.7	3.7	3.7	3.7	3.7	3.7	3.7	3.7	3.7	3.7	3.7

Fig. 43: Development of prevalence/10,000 births with Edwards syndrome in the registration area since 1999

In 2011 one Edwards syndrome (trisomy 18) per 2832 births was registered in Saxony-Anhalt.

12.37 Indicator Malformations, In Total

Indicator malformations are 36 exactly defined major malformations (see definitions in chapter 12.0) by the ICBDSR (International Clearinghouse for Birth Defects). They form a basis for a temporal and spacial comparison of malformation rates on an international level.

We compared in the previous chapters 12.1 to 12.36 the prevalence of each indicator malformation 2011 with the corresponding basic prevalence (1999-2010). Our aim is to identify if the current value differs from the average value.

	Number	Prevalence /10,000 births	Trend in comp. to basic prevalence
Major cities	75	1.57	↘
Districts	139	1.14	↓
Saxony-Anhalt	**214**	**1.26**	↓

Indicator malformations, in total (1999-2010)		
	Basic prevalence /10,000 births	Confidence Interval (CI of 95%) /10,000 births
Cities	1.68	1.57 - 1.79
Districts	1.42	1.37 - 1.48
Region	1.49	1.44 - 1.54

In total, we registered 214 births with indicator malformations in 2011. This corresponds to a percentage of 1.26% of all births from Saxony-Anhalt. At the same time this value of 2011 is lower than every value we observed in the registration period 1999-2010. The total rate and the rate of the districts are clearly under the calculated basis values, the major city rate lies only slightly under the basis values.

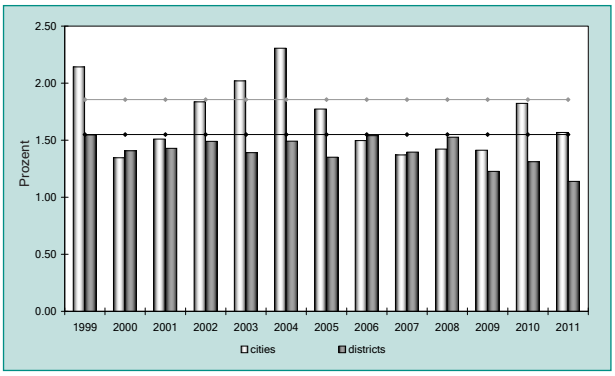


Fig. 44: Indicator malformations of ICBDSR in total (1999 to 2011), comparison of frequency (in %) in the major cities and districts

For the first time we want to analyse in the present report how far the prevalences of indicator malformations changed. Therefore, we analysed a 12-years-trend of the registration period 1999-2011. Condition for the trend analysis is that we expect each malformation to appear at least five times or that we registered at least two cases of the corresponding malformation.

Figure 45 on page 65 shows the average percentage change of each indicator malformation prevalence that corresponds to these conditions in our 12-years-trend analysis. I.e. an increasing trend is illustrated within the positive area (right hand of axis of ordinates) and an decreasing trend is illustrated within the negative area. A significance is only given when the ordinate is not crossed.

We tested the temporary change of the trend-coordinate and the non-linear coordinate for heterogeneity by use of the chi-squared test. We rate the trend as non-linear at a probability of $p > 0,05$ for the linear ratio and $p < 0,05$ for the non-linear ratio. In these cases we did **not** identify a **linear trend**. This applies for **neural tube defects** in total, **spina bifida**, **microcephaly**, **undescended testis** and **preaxial polydactyly**.

To calculate a 12-years-trend change of prevalence on a percentage basis we performed a logistic regression analysis and calculated the regression coefficient B, a value of dimension and direction. To perform this binary logistic regression analysis the maximum-likelihood-estimation is applied. Our diagram shows the annual changes on a percentage basis with a confidence interval of 95%.

The observed trend can be classified as significant at a probability of $p < 0,05$ for the linear ratio and $p > 0,01$ for the non-linear ratio. A **significant decreasing trend**, corresponding to a negative regression coefficient, can be observed for **congenital hydrocephalus**, **cleft lip with or without cleft palate**, **cleft palate**, **small intestinal atresia/stenosis** and for all **indicator malformations in total**.

A **significant increasing trend** shows the malformation **coarctation of aorta** with a value of 6.4% (CI 1.0% to 12.6%) and **anorectal atresia/stenosis** with 7.2% (CI 2.2% to 13.1%) within the registration period 1999 to 2011.
We registered such a significant increase of coarctation of aorta for the first time and we will continue to monitor and analyse its development further on. Here, a possible explication of the increased number of registered cases might be the registration of also small stenoses by means of modern diagnosis procedures.
We analysed in detail the increased number of anorectal atresia/stenosis in Saxony-Anhalt already in our annual report 2010. To identify possible reasons for this increasing trend and to analyse the recorded data, the Malformation Monitoring Centre Saxony-Anhalt cooperates with the Network for Congenital Uro-Rectal Malformations (CURE-Net). Furthermore, we are in charge of a PhD thesis that deals with this topic.

All other indicator malformations do not show a significant positive or negative trend. The chi-squared test gives for the linear and non-linear component a probability of $p > 0,05$. For this reason, the non-linear ratio is not significant and it is also not decisive in regard to a disproportionate increase or decrease.

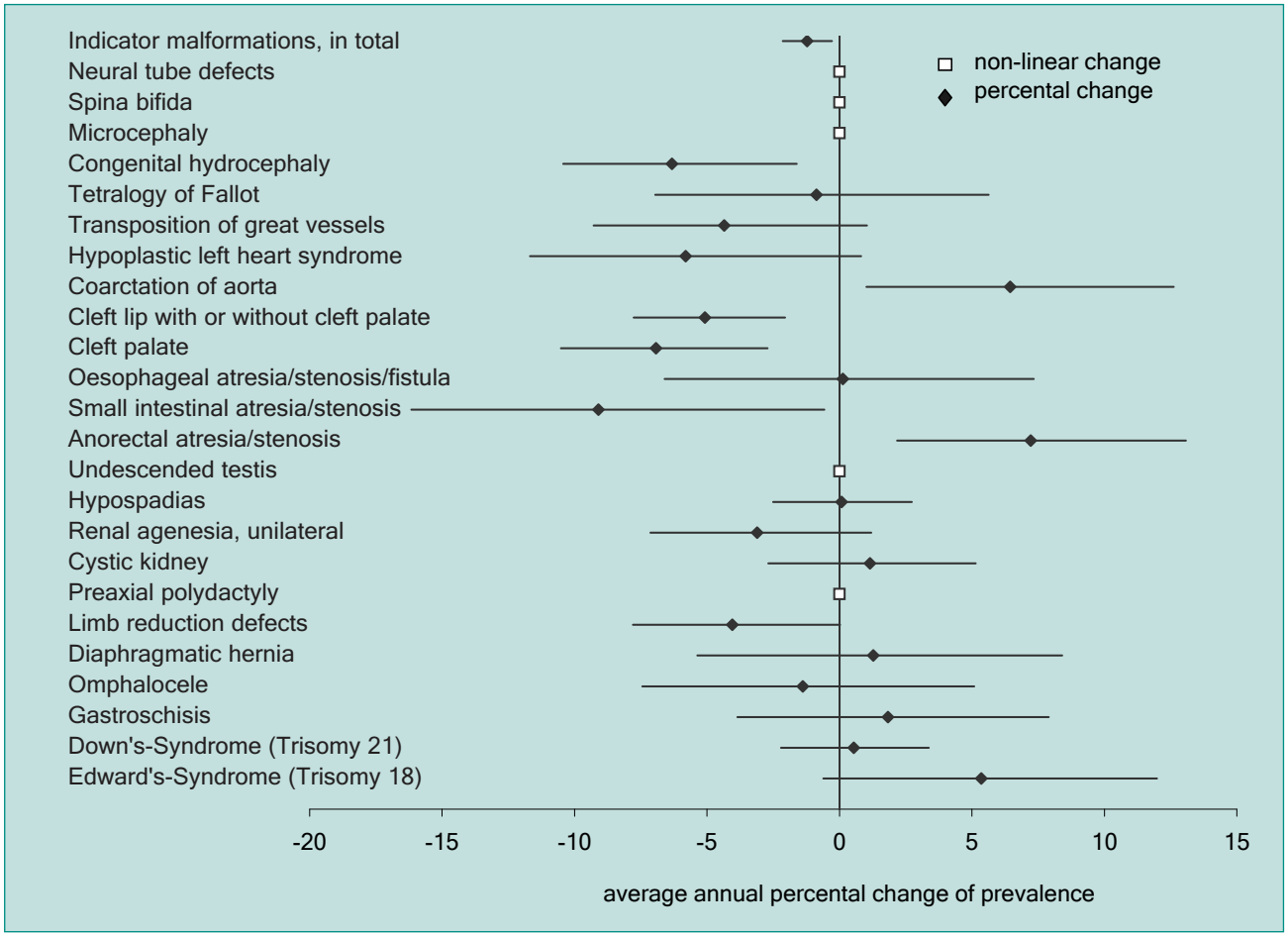


Fig. 45: Trend analysis 1999 - 2011 with average percental change of prevalence per year (95% confidence interval)

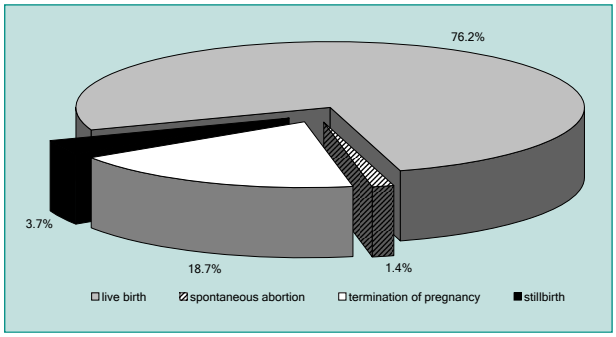


Fig. 46: Pregnancy outcomes of births with indicator malformations 2011

76.2% (163 births) of 214 births with indicator malformations were live births in 2011. Our registered value increased again, however, in contrast the lowest value was registered in 2009 (71.5%). The percentage of 1.4% (3 births) of spontaneous abortions at presence of an indicator malformation continues to be low. However, it slightly increased in comparison to the previous year (1.2%). The percentage of stillbirths (3.7% / 8 births) is higher than in 2010 (1.2%), but similar to the value we registered in 2009 (3.2%).

The rate of terminations of pregnancy at presence of an indication malformation (2011: 18.7%) is slightly under the average value of the last twelve years.

15 Summary

The present annual report 2011 of the Monitoring of Congenital Malformations outlines registered data from Saxony-Anhalt about congenital malformations and anomalies as well as genetically caused diseases. We analysed the registered data statistically and present it now again in the approved manner. Also in this year the analysis of data was made in relation to the population according to the official birth rate provided by the State Statistical Office in Halle.

16,837 infants were live births in Saxony-Anhalt in 2011. In comparison to the previous year the number of live births decreased about 2.7% (2010: 17.300; 2009: 17.144). Related to the live births the number of stillbirths (2011: 69) corresponds to the expected average value of 70 which we also ascertained during the registration period 1999-2010.

According to the Federal Statistical Office 662,685 infants were live births in Germany in 2011 (2010: 677.947; 2009: 665.126). Only 2.5% of these births were born in Saxony-Anhalt in 2011.

The Monitoring of Congenital Malformations registered among data of life and stillbirths 58 terminations of pregnancy and 25 spontaneous abortions after 16 weeks of gestations. The prevalence calculations therefore are based on a total number of 16,989 births (see chapter 2).

537 births had at least one major malformation. This corresponds to a percentage of 3.16%. The malformation rate decreased in comparison to the previous year (2010: 3.38%), but it continues to be on a constant level in our 12-years-trend analysis (see chapter 8).

87.71% of infants with a major malformation were live births in 2011 (2010: 86.95%; 2009: 86.72%). In 9.68% of the cases a termination of pregnancy took place in 2011. This percentage ranges between 7% and 12% since the end of the nineties. The number of spontaneous abortions is very low in comparison to the previous years (0.74%) however, the rate of stillbirths of 1.86% is very high. The number of stillbirths in 2011 is the highest value we registered since 1992 (see chapter 7 and 8).

When analysing the frequency of appearance of single diagnoses in 2011, it shows as expected that atrial septal defect and ventricular septal defect are the most frequent and second most frequent single malformations. These two cardiac malformations are followed 2011 by dilatative uropathy and haemodynamic relevant PDA, which we registered considerably more often than in the previous years. Position four to seven of the most frequent single diagnoses 2011 are occupied by Down's syndrome, clubfoot, congenital hearing disorder and polydactyly.

1.25% of all births 2011 suffered from an indicator malformation. This is the lowest value we observed since 1997 (see chapter 12). We calculated in 2011 for the following indicator malformations higher rates in regard to the corresponding basic prevalence: transposition of great vessels, undescended testis and Prune-belly-sequence. We calculated lower rates in comparison to the basic prevalence for anencephalus, spina bifida, microcephalus, congenital hydrocephalus, arhinencephaly / holoprosencephaly, microtia / anotia, tetralogy of fallot, cleft lip with or without cleft palate, cleft palate, small intestinal atresia and stenosis, hypospadias, preaxial polydactyly and diaphragmatic hernia. The rarely occurring indicator malformations epispadias, indifferent sex and bladder exstrophy were not registered in Saxony-Anhalt in 2011.

Furthermore, we registered data about 53 pregnancys with a prenatally confirmed malformation of the foetus which led to a termination of pregnancy. More than 50% of the terminations of pregnancy took place due to presence of a chromosomal aberration (50,9 %). Only in four cases (7.6%) the termination of pregnancy was induced due to presence of a malformation of the central nervous system, which is a very low number.
96,2 % of all terminations of pregnancy took place before 23 weeks of gestation.

24 infants and foetuses suffered in 2011 from a genetically caused disease. However, in comparison to the previous year, more concerned infants (83.3%) were born alive (2010: 64,3 %; 2009: 61,8 %). In 18 cases a sequence, association, resp. complex was diagnosed. At eight births a embryopathy or congenital infection occurred. Reason for the embryopathy was a maternal gestational diabetes resp. diabetes mellitus. The average maternal age of 43 births with chromosomal aberration was slightly lower (33.7%) than in the previous years. The percentage of mothers aged over 35 was with a value of 39.5% rather low.

Chapter 16 of the present annual report deals with the topic neural tube defects. The folic acid prophylaxis continues to be an important matter in this relation. Also after 20 years of a periconceptional folic acid intake recommendation, the trend analyses does not show a regressive trend of appearance.

In 2011 the Monitoring of Congenital Malformations received data from 1805 births from Saxony-Anhalt. At least one major malformation occurred at 537 births. In 251 cases only minor malformations or anomalies were registered. The Monitoring of Congenital Malformations registers at the one hand data about infants and foetuses with congenital malformations and on the other hand data about infants without malformations as control cases. These control cases are necessary as the risk calculation in a scientifically founded analyses is only possible when comparing both groups.

Compilation of the present 2011 Annual Report was only possible due to ongoing voluntary reports about congenital malformations from various medical institutions of Saxony-Anhalt. We would like to thank all "senders" and hope that this excellent cooperation will continue!

16 Neural tube defects (NTDs)

Definition

The term neural tube defect designates a range of malformations of the central nervous system which are formed due to a disorder in the structural development of the neural tube. In case of a normal development, the neural tube closing process is finished after 28 days post conception. This closing does not take place, as formerly believed, like the closing of a "zipper", but the neural tube closes at different positions and at different points of time. Therefore, various phenotypes exist: myelomeningocele, anencephaly, encephalocele, lipomeningocele, meningocele, iniencephaly, cloacal extrophy.

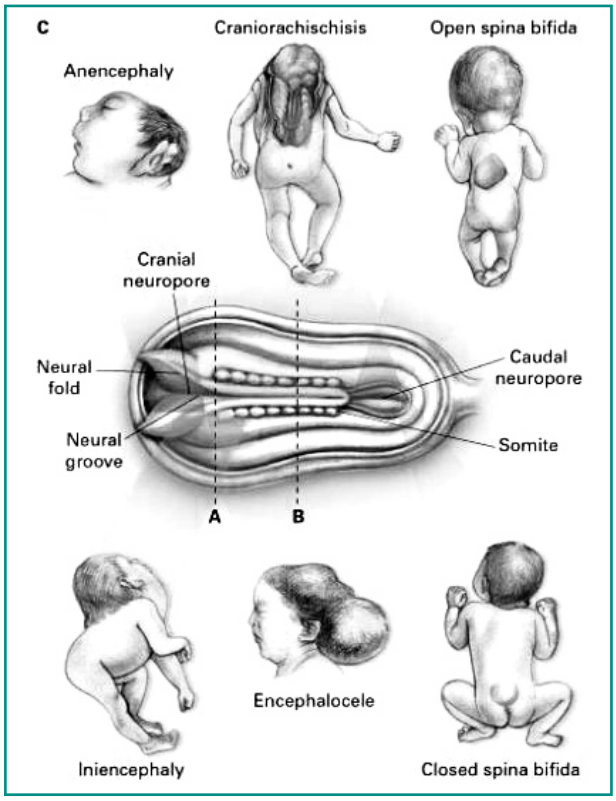


Fig. 49: Classification of the neural tube defects
modified acc. to Botto et al. (1999) Fig.1, page 1510

The myelomeningocele, lipomeningocele and meningocele have the highest probability of surviving. The lowest probability of surviving is given when patients suffer from anencephaly and/or craniorachischisis. These are very severe defects where parts of the brain and spinal canal are translocated to the outside.

Neurulation = embryonal neural tube development

The primary neurulation starts in the third week after conception with formation of the neural plate from the ectoderm. The neural plate is induced by the chorda dorsalis and the adjacent mesoderm. Pressure of the expanding epidermis causes the neural plate to fold resulting in neural folds and the creation of the neural groove. The neural folds form dorsolateral hinge points (DLHP) and pressure on this hinge causes the neural folds to meet and fuse at the midline. The primary neurulation terminates with the closure of the neuropore anterior on day 24 and posterior on day 26. At the caudal neuropore the neural tube is formed by accumulation of mesenchymal cells and subsequent canalisation. This process is called secondary neurulation.

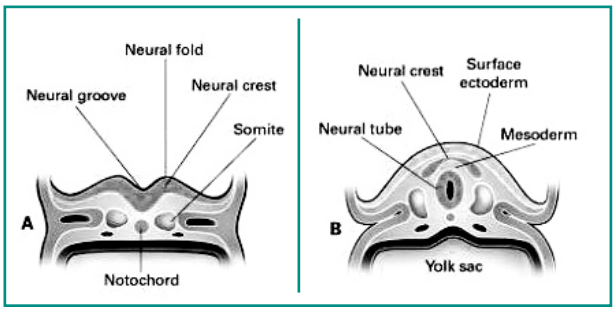


Fig. 50: Neural tube development
modified acc. to Botto et al. (1999), fig. 1, page 1510

Classification - Spina bifida aperta

Myelomeningocele, meningocele and lipomeningocele are often called "spina bifida aperta" or in the clinical context they are just called "spina bifida".

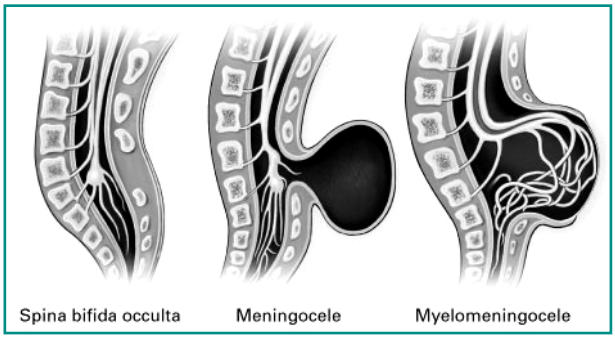


Fig. 51: Different types of Spina bifida
Botto et al. (1999), fig. 2, page 1511

Spina bifida occulta leads only to an osseous defect and does not show any neurological dysfunction. Therefore it is not mentioned separately within epidemiological analyses. The mildest form of a dorsal gap formation is the normally lumbosacral located dermal sinus. It is not classified as neuropediatric disease but a problem when patients suffer from this malformation might be the ascension of germs.

Different populations show a frequency of appearance of spina bifida aperta among the neural tube defects up to 70 %. The following table shows the ratio of the different phenotypes we extracted from our data.

Period of time 1980-2011	Number	Percentage (%)
Encephalocele	55	11.5
Anencephaly	130	27.1
Spina bifida	294	61.4

Spina bifida aperta still appears as a complex neuronal malformation and therefore it presents an interdisciplinary challenge during the medical treatment of the patients in the hospital. The postnatal mortality lies worldwide still at 10%.

Spina bifida aperta - important aspects of clinical symptoms

- extent of the dysfunction is not congruent to the location of the lesion = level of the spinal damage (paraplegia)
- a typical symptom is an asymmetric diverging sensory and motoric level of paralysis because neuronal tissue was primarily damaged
- therefore it is important to detect the individual level of paralysis
- for this purpose the spontaneous motor activity and innervation of reference muscles have to be observed, additionally the sensitivity in relation to the age of the child has to be checked
  (Attention: below the spinal damage often paresis is present but by spinal automatisms provoked muscle contractions are possible!)
- 80-90% of patients suffer from a congenital hydrocephalus or develop such anomaly during the first year of age
- Chiari-malformation type II is present in 90% of the cases (with cerebellar herniation through foramen magnum)
- association with corpus callosum dysgenesis
- neurogenic voiding dysfunction of bladder and intestine (depending from the level of the spinal damage)
- hip dysplasia and limb deformity caused by neurological disorder
- cognitive restrictions and behavioural problems
- primary or secondary tethered cord, syringomyelia
- sexual dysfunction
- latex allergy

Etiology of neural tube defects

- mainly not appearing in combination with typical syndromes
- but infrequently syndromes appearing in combination with NTDs: Meckel-Gruber syndrome, Waardenburg syndrome, Jarcho-Levin syndrome
- possible associations with NTDs: OEIS complex (omphalocele-exstrophy-imperforate anus-spinal defects), VACTERL association, caudal regression syndrome, Klippel-Feil syndrome, Joubert syndrome
- approximately one child out of five with NTD suffers from an additional malformation, often from a midline anomaly
- chromosomal aberrations appending with NTDs (trisomy 13, trisomy 18))
- multifactorial origin: conjunction of environmental influences and genetic causes
- environmental influences: maternal diabetes / impaired glucose metabolism and obesity, maternal alcohol intake or intake of anti-epileptic drugs (Valproat, Carbamazepin), folic acid antagonists
- genetic causes: it was possible to identify genes which are involved in the neural tube development with 240 mouse mutants
- various mutations which are directly related to the folic acid metabolism, e.g. methylentetrahydrofolate reductase (MTHFR), polymorphism with thermolabile enzyme and homocysteinemia (MTHFR catalyses the formation of 5-methyltetrahydrofolate [Metafolin] which is the biologically active form of folic acid)
- the curly-tail mouse presents a prototype of the folic acid "independent" appearing spina bifida, here myo-inositol substitution is invented as prevention measure

Origin of folic acid prevention

- **1965 Hibbard & Smithells** describe a connection between the maternal folate status and congenital malformation occurrence
- **1991 MRC-Study Group** provides evidence that folic acid intake reduces the risk of recurrend NTD
  (first international double blind randomized study)
- **1992 Czeizel & Dudas** proof periconceptional folic acid intake as primary prevention for NTD
  (randomized study in Hungary; placebo = supplement with microelements, verum = supplement with combination of multivitamins and micoelements)
- **1999 Berry et al.** publication of first intervention studies
  (1993-1995 intake of 0,4 mg/d folic acid led to a reduced appearance of NTDs in the high risk area of northern China up to 85%. In the lower prevalence area of south China a reduction up to 40% was observed.)
- **2010 Cochrane meta-analysis** confirmed protective effect of the daily periconceptional intake of folic acid to prevent a NTD and did not indicate any negative impact
  (studies including folic acid doses of 0.36- 4 mg with and without additional intake of vitamins and minerals)

Folic acid prophylaxis

Study results of different populations show that 70% of NTDs in humans respond to a folic acid supplementation, but 30% of these defects are folic acid „resistant“ during their development.
However, despite the possibility of a proven affordable primary NTD prevention we do not nearly reach the scientifically proven possibilities of a reduction of this malformation in Europe.
There are no such Programs to fortify staple food with folic acid in European countries like in North and South America.

Different food is fortified with folic acid on a voluntary basis in Germany, only salt, in addition there are baking mixtures, breakfast cereals and juices. In North America, South America and in parts of the Middle East the government prescribed that their flour has to be fortified with folic acid. Such implementations did not take place in any European country.

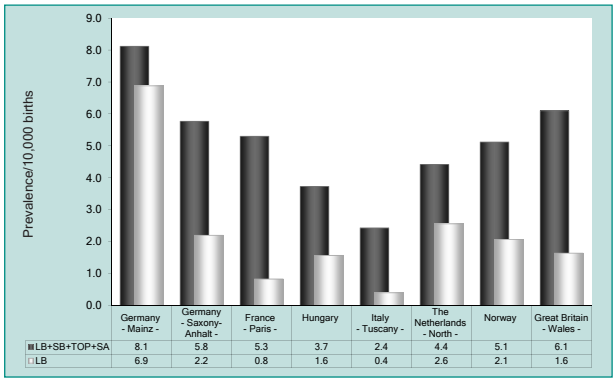
Recommendations regarding folic acid prophylaxis

Since 1995 different German Associations, including the German Society of Paediatrics and Adolescent Medicine and the German Society of Obstetrics and Gynaecology have the following recommendations regarding the folic acid prophylaxis:

- **women of childbearing age** should take additionally **0.4 mg per day folic acid / folic acid equivalent**
- **women who already had a pregnancy with NTD** should take additionally **4 mg per day folic acid / folic acid equivalent**
- **start** of the intake should be at least **4 weeks prior to conception and last up to 12 weeks after conception**

Epidemiologic data

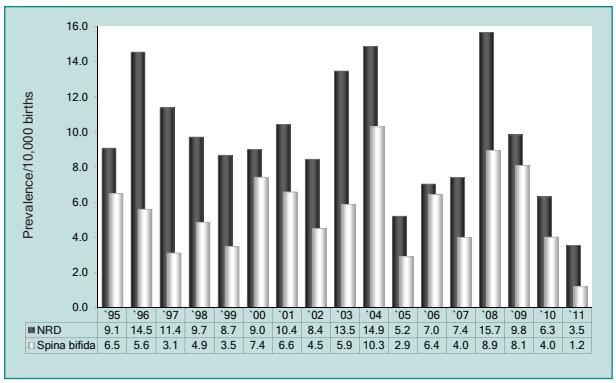
The current frequency of appearance of spina bifida varies in different populations. Worldwide approximately 400,000 infants are born annually with spina bifida aperta. The following table shows the total and life births prevalence of some regions / countries for spina bifida (2005-2009).



	Germany - Mainz -	Germany - Saxony-Anhalt -	France - Paris -	Hungary	Italy - Tuscany -	The Netherlands - North -	Norway	Great Britain - Wales -
LB+SB+TOP+SA	8.1	5.8	5.3	3.7	2.4	4.4	5.1	6.1
LB	6.9	2.2	0.8	1.6	0.4	2.6	2.1	1.6

Fig. 52: Total and life births prevalence of spina bifida in Europe (extract) 2005-2009

EUROCAT data (analyses of prevalences of 21 European registries, 4 million births 1999-2008) show for the first time in a 10 years-trend-analyses a declining trend of neural tube defects (4.5% / 2 years intervalls) and spina bifida (5.7% / 2 years intervalls) in Europe.
This raises the question of weather we already reached the maximum possible success of the folic acid prophylaxis in Europe.



	`95	`96	`97	`98	`99	`00	`01	`02	`03	`04	`05	`06	`07	`08	`09	`10	`11
NRD	9.1	14.5	11.4	9.7	8.7	9.0	10.4	8.4	13.5	14.9	5.2	7.0	7.4	15.7	9.8	6.3	3.5
Spina bifida	6.5	5.6	3.1	4.9	3.5	7.4	6.6	4.5	5.9	10.3	2.9	6.4	4.0	8.9	8.1	4.0	1.2

Fig. 53: Development of prevalence / 10,000 births since 1995 for neural tube defects and spina bifida in Saxony-Anhalt

Data from Saxony-Anhalt

The trend analyses of our data for neural tube defects and spina bifida in Saxony-Anhalt (1995-2011) does not show a linear course. This means that we did not record a proven effect of success since the beginning of propagation of folic acid intake. These results are congruent to the findings of our colleagues in Mainz. (Mainzer Modell). Encephalocele were not analysed as their frequency of appearance was too low.

Limit of the pericenceptional folic acid

The main factor are unplanned pregnancys (studies recorded for eastern Germany a rate of 47 % of unplanned pregnancies and for western Germany a rate of 29 %. The highest rate of unplanned pregnancys of 75 % was recorded among women aged between 16 and 19).

Additionally, the time frame for the intake of folic acid is very small, only up to day 28 post conception. Also women who plan a pregnancy mainly stop to take the oral contraceptive on their own and attend their gynaecologist not until their mens was absent for one or two months. In these cases 5 to 7 weeks of gestation might have passed and the critical time frame of four weeks when the neural tube closes have already passed.

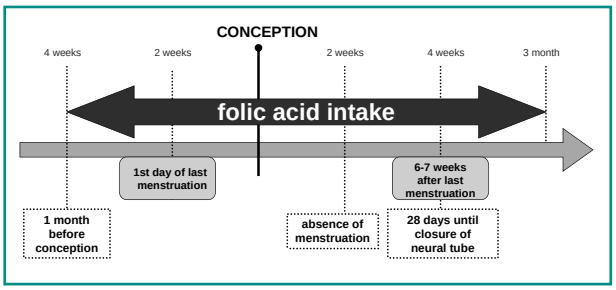


Fig. 54: Process of folic acid prophylaxis

Compliance?

Studies published on this topic show a close relationship between the reduction of NTD risk and the maternal folate status. That means that a higher folate status, also in case of incomplete compliance is beneficial for the fetus in every case.

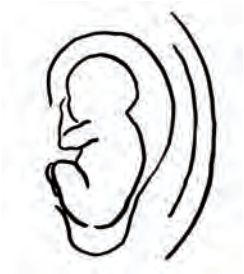
Perspective of folic acid prophylaxis

There are serious hints about further positive effects in connection with folic acid intake such as a reduced rate of conotruncal heart defects and oral cleft formation. However, these effects could not be verified until now in randomised studies. Nevertheless, on the basis of the already recorded data, the WHO is convinced about the positive effects of NTD prevention for the pregnancy outcome and outlined this in their latest guideline publication "Intermittent iron and folic acid supplementation in non-anaemic pregnant women". To ban a relevant genetic risk factor (MTHFR gene polymorphism) for the formation of NTDs by the intake of folic acid many modern drugs nowadays contain Metafolin which is the biological active form of folic acid.

Conclusion

At the beginning of the 21st century the hope for a significant reduction of the NTDs / spina bifida was nearly euphoric, as the burden for children and their families who were affected by this malformation was heavy. But this hope could not be fulfilled. The current challenge for doctors in the hospitals and also for the public health sector is now to find out how the scientific results on primary prevention of NTDs can be better implemented into everyday life. To end up with an increased number of TOP after improved prenatal diagnosis is not the aim in prevention. These tasks have to be solved not only by the German public health sector but also by the European and even International Health Community.

Indication of source:
Botto, L. D.; Moore, C. A.; Khoury, M. J.; Erickson, J. D. (1999): Neural-tube defects. In: N Engl J Med 341 (20), p. 1509-1519
further literature in possession of the author



18 Newborn Hearing Screening 2011

Introduction

A general newborn hearing screening belongs as from the 01-01-2009 to the recommended early detection examinations after the birth of a child.
Aim of the newborn hearing screening is to detect congenital hearing disorders at an early stage (up to the 3rd month of life) and to initiate the corresponding therapies (up to the 6th months of life).

Basis for this early detection examination is “Enclosure 6 - early detection examination of hearing disorders at newborns (newborn hearing screening)” of the Children Directive issued by the Federal Joint Committee (G-BA) on 19-06-2008.

The Children Directive determines the process of the newborn hearing screening in the following way:
- measurement of each ear by TEOAE or AABR up to the third day of life (outside of hospital by no later than early detection examination 2 (U2))
- for children at risk AABR examination is mandatory
- examinations of premature infants by no later than calculated date of delivery and examinations of not healthy newborns by no later than third month of life
- at suspicious first screening, repetition of examination at both ears by AABR preferably on the same day, but by no later than early detection examination 2 (U2)
- at suspicious finding of the follow-up examination by AABR comprehensive confirmation diagnostics is necessary up to the 12th week of life

According to the Children Directive performance and results of the newborn hearing screening as well as a possible confirmation diagnostics have to be recorded in the “yellow book of examination” of every child. The responsible paediatrist resp. ENT physician can evaluate by this information if the required diagnostics resp. therapy in case of a hearing disorder was initiated.

The Malformation Monitoring Centre Saxony-Anhalt cooperates with the Center for Newborn Hearing Screening Saxony-Anhalt since 2006 as tracking center for the newborn hearing screening (Federal State dependent screening centre).

The Newborn Hearing Screening Directive stipulates that the hearing screening should be performed via AABR at children with an increased risk for congenital hearing disorders. The following overview outlines in extracts possible indications for the performance of an AABR examination due to an increased risk of hearing disorders (modified according to JCIH 2007*):
- positive family history regarding a hearing disorder
- clinical suspicion of hearing disorder/deafness
- premature birth, births weight under 1500 g
- neonatal intensive care
- hyperbilirubinemia (exchange transfusion)
- pre-, peri- or postnatal hypoxia
- peri- and postnatal cerebral hemorrhage, oedema
- intrauterine infections
- culture positive postnatal infection associated with increased risk of hearing loss
- craniofacial anomalies
- distinctive diseases with hearing loss
- neurodegenerative diseases or sensomotoric neuropathies
- outer characteristics, which point to a distinctive disease that appears in combination with a hearing disorder (e.g. white strand of hair)
- APGAR-values of 0-4 in the first minute and/or 0-6 after 5 minutes

* Joint Committee on Infant Hearing (JCIH):
Year 2007 Position Statement: Principles and Guidelines for Early Hearing Detection and Intervention Programs. Pediatrics. 120. 898-921 (2007) DOI: 10.1542/peds.2007-2333

Participating Institutions

In 2011 we had 27 materny clinics in Saxony-Anhalt. In all of these clinics a long term newborn hearing screening was and is offered mainly by TEOAE. In 2011 all of these clinics participated in the tracking.
A Screening ID is assigned to each child - if there is no denial of this examination and/or data transmission by parents/guardians - and the hearing screening results will be forwarded to the tracking center for the newborn hearing screening in Saxony-Anhalt.

The screening ID, which has to be assigned to each infant as condition to participate in the hearing screening trakking is also used by several midwifes. In this way also infants who are exclusively under care of a midwife (e.g. home births) can participate in the newborn hearing screening.
The following table on page 82 gives an overview about the single materny clinics and number of births with a screening ID.

Materny clinics in Saxony-Anhalt and participation in the Newborn Hearing Screening Tracking (ordered by location)

Materny clinics	Tracking period 2011	Births in this period*
Ameos Klinikum Aschersleben	01-01 to 31-12-2011	567
Ameos Klinikum Bernburg	01-01 to 31-12-2011	293
Gesundheitszentrum Bitterfeld/Wolfen gGmbH	01-01 to 31-12-2011	450
Krankenhaus Jerichower Land GmbH Burg	01-01 to 31-12-2011	380
Städtisches Klinikum Dessau	01-01 to 31-12-2011	790
Altmark-Klinikum gGmbH Krankenhaus Gardelegen	01-01 to 31-12-2011	336
Ameos Klinikum St. Salvator Halberstadt	01-01 to 31-12-2011	549
Sana Ohre-Klinikum GmbH Haldensleben	01-01 to 31-12-2011	279
Krankenhaus St. Elisabeth und St. Barbara Halle	01-01 to 31-12-2011	1.816
Universitätsklinikum Halle (Saale)	01-01 to 31-12-2011	1.061
Krankenhaus Köthen GmbH	01-01 to 31-12-2011	373
Klinik St. Marienstift Magdeburg	01-01 to 31-12-2011	789
Klinikum Magdeburg gGmbH	01-01 to 31-12-2011	1.076
Universitätsklinikum Magdeburg A.ö.R.	01-01 to 31-12-2011	1.256
Carl-von-Basedow-Klinikum Saalekreis GmbH Merseburg	01-01 to 31-12-2011	682
Saale-Unstrut Klinikum Naumburg	01-01 to 31-12-2011	349
Bördekrankenhaus GmbH Neindorf	19-02 to 31-12-2011	206
Harzklinikum Dorothea Christiane Erxleben GmbH Quelinburg	01-01 to 31-12-2011	543
Altmark-Klinikum gGmbH Krankenhaus Salzwedel	01-01 to 31-12-2011	372
Helios Klinik Sangerhausen	01-01 to 31-12-2011	781
Ameos Klinikum Schönebeck	01-01 to 31-12-2011	438
Johanniter-Krankenhaus Genthin-Stendal gGmbH	01-01 to 31-12-2011	893
Asklepios Kliniken Weißenfels-Hohenmölsen GmbH	01-01 to 31-12-2011	437
Harz-Klinikum Wernigerode-Blankenburg GmbH	01-01 to 31-12-2011	586
Evangelisches Krankenhaus Paul Gerhardt Stift Wittenberg	01-01 to 31-12-2011	586
Georgius-Agricola Klinikum Zeitz	01-01 to 31-12-2011	353
Krankenhaus Anhalt-Zerbst gGmbH	01-01 to 31-12-2011	233
Total number of births* in Saxony-Anhalt		**16,519**

Home births / Births in a birthing centre resp. infants not born in Saxony-Anhalt	01.01. - 31.12.2011	**151**

Tracked infants, in total	**16,670**

* births + multiple births, in case no number was assigned by the birth register, number of stillbirths is deducted

In total, **16,519 births** received a screening ID in a materny clinic in Saxony-Anhalt in 2011. Therefore, these infants participated in the hearing screening tracking. Furthermore, **151** data records of **children** which were home births or born in a birthing centre are included in the analyses. These infants received also a screening ID after birth, e.g. by the corresponding midwife.

Tracking Effort

Tracking of the newborn hearing screening requires an ample organising and personnel effort. The materny clinic has to record the results of the hearing test and forward them by mail or fax to the Malformation Monitoring Centre Saxony-Anhalt. The results are entered here in a special tracking database. In total, we received results of **104 senders** in 2011.

The following table shows how much newborns received a screening ID per month and and how many results were forwarded to the Monitoring of Congenital Malformations per month. Averagely, at least 1,800 results are reported per month, however in some cases we receive multiple reportings for one child (e.g. from the materny clinic, paediatric clinic, ENT clinic, ENT physician, paediatrist and from the parents).

Births with screening-ID and number of incoming result

2011	Infants with screening ID	Number of reportings
Januar	1,374	1,880
Februar	1,284	1,774
März	1,341	1,753
April	1,208	1,598
Mai	1,315	1,750
Juni	1,466	1,942
Juli	1,562	1,987
August	1,535	2,032
September	1,484	2,004
Oktober	1,438	1,818
November	1,299	1,696
Dezember	1,364	1,722
gesamt	**16,670**	**21,956**

To carry out the tracking thoroughly, **2,538 letters** were forwarded in 2011 (one up to seven letters per infant). With reference to all infants with screening ID this corresponds to an average of 0.15 letters per infant.

Additionally, the parents were contacted by telephone. In total **266 calls** were made in the course of the hearing screening tracking (one up to three calls per infant).

Results

All results, that were reported to the hearing screening tracking centre are included in the analyses of the newborn hearing screening:

13,950 infants out of **16,670 infants** with screening ID had an **unsuspicious newborn hearing screening**.
In **2,720 cases** the **first hearing test had to be followed-up**, resp. no newborn hearing screening took place in the materny clinic (these cases are regarded also as follw-up cases). There are numerous reasons why a hearing test did not take place, e.g. ambulant delivery, early discharge from materny clinic, transfer of the child to another clinic or a defective hearing screening device.

The **follow-up examination** of the 2,720 infants showed in **2,119 cases** an **unsuspicious result**. The remaining **601 infants** had again a **suspicious result**. **132** of these 601 infants received a **complete paediatric audiological confirmation diagnostics**.
According to our knowledge, **169 infants** did **not receive a confirmation diagnostics** and therefore are considered as **lost to follow up**.

264 infants did **not participate in the screening** (no reaction of parents to reminder letters or refusal of examination) and in **seven cases** the **status** is still **pending**, i.e. the examinations were not finished in August 2012 or the trakking process still requires more time.
In **29 cases** the **tracking** was finished from our side **without any result**.

In total, the **follow up-examinations** of **147 infants** who were born in 2011 could be completed. Among 132 infants with a suspicious result, 11 infants had an unsuspicious first screening. Maybe these infants received a follow-up-examination due to present risk factors. Within the follow-up examination, a **hearing disorder** could be **excluded** in **101 cases**, in **31 infants** a unilateral/bilateral **hearing disorder was diagnosed** and the corresponding therapy was initiated. For instance, **19 infants** received a **hearing aid** (9 times hearing aid bilateral, 10 times hearing aid unilateral).

19 Annual Report 2010 of the Newborn Screening Centre Saxony-Anhalt

according to §14 Note 2 of the valid Children Directive

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Competence net newborn-screening

Berlin • Greifswald • Magdeburg • Weiden

Introduction

In 2011 the Federal Joint Committee of physicians and health insurances (G-BA) accepted the screening report of the German Society of newborn screening (DGNS) as valid form of an annual report. Therefore, only one form of report will exist in the future which makes the work of the screening laboratorys considerably easier.

10 out of 18 suspicious cases for endocrine and metabolic diseases (positive first screening and follow-up screening) could be confirmed by the corresponding confirmation diagnostics. The care by a metabolic centre or an endocrinologist as well as the implemented therapy was monitored and documented.

Our screening laboratory obtained also in 2011 all required certificates for an external quality control of all parameters that are examined during the screening (CDC Atlanta, Deutsche Gesellschaft für Klinische Labordiagnostik).

The number of senders slightly increased in this year, from 225 in 2010 to 240 in 2011. 26 inpatient institutions, 122 physicians in private practice and 92 midwifes send blood tests to our screening laboratory in Magdeburg.

The annual meeting of all senders took place on 15 January 2011. Due to this early date in January 2011 the number of attendants (49) decreased but we were anyway happy about every participant. We discussed the implementation of the Gene Diagnostics Act by midwifes in private practice and listened to a special case presentation (BH4 deficiency). Another topic was apart from the usual analyses of statistics and the discussion of problems, cases of paediatric metabolism emergencies caused by congenital metabolic disorders. The lecture about this topic was held by Prof. Dr. Eberhard Mönch of the Charité Berlin.

Screening Amplitude

The screening amplitude in Saxony-Anhalt has not changed in comparison to the previous years (PKU, hypothyroidism, CAH, galactosemia, biotinidase deficiency, enlarged screening "TMS"). The used methods, reference levels and recall- and detection rates are illustrated in the following two tables:

Tab. 1: Methods/analytics 2011

Parameter	Disease	Method	Reference Value
TSH	Hypothyroidism	Fluorescence immunoassay	<15 mU/l
GALT	Galactosemia	fluorometric	>3.5 U/gHb
BIO	Biotindase deficiency	enzymatic	normal/reduced activity; qualitative method
17OHP	Congenital adrenal hyperplasia (CAH)	Fluorescence immunoassay	depends on gestational age
AC*	see annotation	TMS***	99.9th resp. 0.1th percentile of the normal distribution
AS**	see annotation	TMS***	99.9th resp. 0.1th percentile of the normal distribution

AC* Acylcarnitine - Group of parameter to recognize fattyacid oxidation disorders, organoaciduria and carnitine cycle defects
AS** Amino acids - to recognize aminoacidopathy (PKU, MSUD)
TMS*** Tandem-mass spectrometry

Examination Numbers, Recall Rates and Assured Cases

Table 2 shows the recall rates of the single parameter and the assured cases. In otal, 148 recalls had to be done in 2011.

Tab. 2: Samples, assured cases, recall-rate 2011

	First test	Second test*	Recall rate** 2010	Assured Cases	Incidence in Saxony-Anhalt 1992-2010
TSH	16,666	560	0.05 %	4	1/3,720
PHE***	16,666	560	0.03 %	4	1/5,486
GALT	16,666	560	0.01 %	-	1/144,961
BIO	16,666	560	0.01 %	1	1/206,307
17OHP	16,666	560	0.28 %	-	1/22,072##
AC, AS (TMS)	16,666	560	0.04 %	1 x LCHAD#	1/100,713###

* Second transmissions, which were necessary because of an early blood withdrawal at term infant < 36 h or preterm infant < 32 weeks of gestation resp. positive first result (recall)
** Definition of recall: demand of a new blood sample because of a suspicious screenig result, when the first test took place at an age of > 36 h at term infant or >32 weeks of gestation at preterm infant
*** Phe = phenylalanine: parameter for the identification of a phenylketonuria and hyperphenylalaninemia
# MCAD: disorder in metabolizing medium-chain fatty acids
Screening of congenital adrenal hyperplasia syndrome (since 1997 in Saxon-Anhalt)
Enlarged screening (TMS) since May 2001 in Saxony-Anhalt

Registration Rates

We collected the following registration rates in Saxony-Anhalt in 2011: According to the Federal Statistical Office 16,837 children were live births in Saxony-Anhalt (according to residence of the mother).

Tab. 3: Registration rates of first tests

	Number	Difference/sum
first screening in Magdeburg	16,666	
not resident in Saxony-Anhalt	680	15,986
Screening refused by parents resp. probably not shown up for U2, no response	4	15,990
screening in another Federal State*	18	16,008

* only infants were counted whose mother had a residence in Saxony-Anhalt

The discrepancy between the number of livebirths and screened infants mounts to 829.

The data of the Federal Statistical Office are based on the data of the Statistical Office of Saxony-Anhalt. All births (sorted according to maternal residence) that are reported by the materny clinics to the register office form the basis here. However, the number of mothers with residence in Saxony-Anhalt but who delivered their infants in another Federal State is not recorded in our screening statistics when the screening of the infant took also place in the other Federal State. Infants with screening in another Federal State but who are resident in Saxony-Anhalt are only regarded when a clear assignment was assured afterwards.

The control of second examinations showed the following result: All 588 necessary second examinations (including controls of positive first transmissions) were tracked.

Tab. 4: Registration rates of second tests

	Early withdrawal <36 h.	Preterm infants <32 WOG	Controls of positive first transmissions
Second screening necessary: **588**	331	205	52*
Control in the own laboratory: **560**	319	190	51
Descended before second Screening	-	14	1
Screening in another Federal State	9	1	-
remaining	3	-	-

* here only real recalls (first transmission >36 h, > 32 WOG)

The children who were screened in another Federal State live in most cases at the border between two States, the blood withdrawal was done by midwifes or physicians in private practice who did not send the blood samples to Magdeburg. One preterm infant was transferred to a specialist hospital where also the second screening took place.

The Permanent Committee of the Newborn Screening of the Working Group for Paediatric Metabolic Disturbances (APS) and for Paediatric Endocrinology (APE) of the German Society of Pediatrics and Adolescent Medicine, the German Society of Neonatology and Paediatric Intensive-Care Medicine (GNPI) and the German Society of the Newborn Screening (DGNS) in collaboration with the German Society of Gynaecology and Obstetrics (DGGG) and the German Society of Perinatal Medicine (DGPM) demand in their Directive of 2002 that a required secondary examination should be generally done by the original responsible screening laboratory. Thereby, the screening process should be

be easier to control. Unfortunately, this is not possible in every case.

Process Times

Point of Taking Blood Samples

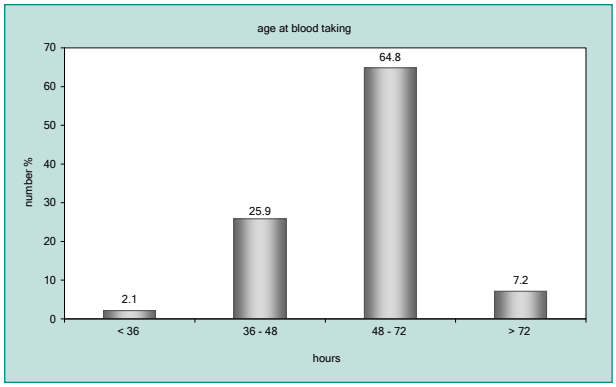

Fig. 1

The optimal point of taking blood samles for the newborn screening (36 -72 hours of life) took place within the required period of time at 90.7% of all cases. At a total number of 9.3% the taking of blood samples took not place within the required period of time (2010: 7.1%). The data of 2011 changed for the worse in comparison to the previous year.

Note: Data of a newborn infant was only registered when all required information was given (date of birth and time as well as date of blood taking and time).

Transmission Time

Figure 2 shows that 37.1% of all transmittals reached the laboratory after more than two days after the blood taking (2010: 37.4 %). 3.97% of all blood samples needed more than four days (2010: 3.4 %).

Problems with the transmission occurred also in 2011, these are comparable to the problems we faced in 2010. The Children Directive requires the transmission of a pathological result by the laboratory to the sender by no later than 72 hours after the blood taking. The limiting factor is here the time from the blood taking up to the receipt of the blood sample (delivery time). In this connection we want to point out again that the Children Directive requires a transmission of each blood sample at the day of withdrawal.

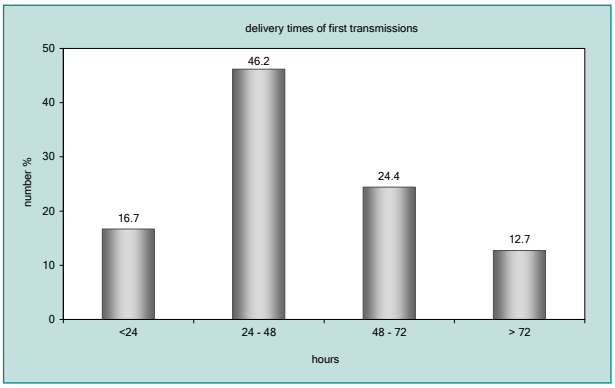

Fig. 2

Transmission of Results

Figure 3 shows the age of the children at the point of result transmission. These data are influenced very much by the time of blood taking, delivery time and time of diagnostics.

At 2.0% (2010: 1,4 %) of all newborns, the screening result was present only after 8 days of life. In an extreme case, e.g. a typical galactosemia such a result may be too late and the infant might have died. Most blood samples were taken within the required period of time, however they reached the laboratory delayed.
In such cases the laboratory calls the attention of the sender by mentioning a corresponding note on the result. This is a try to improve the process in this way.

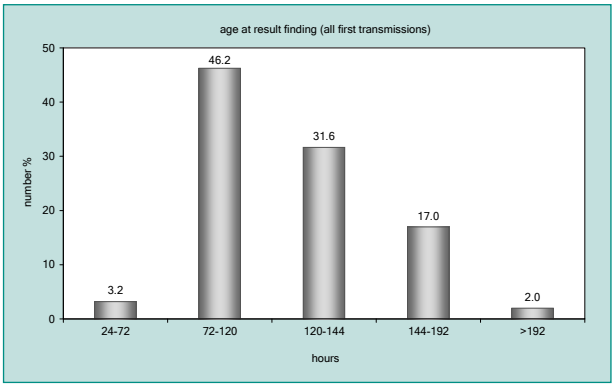

Fig. 3

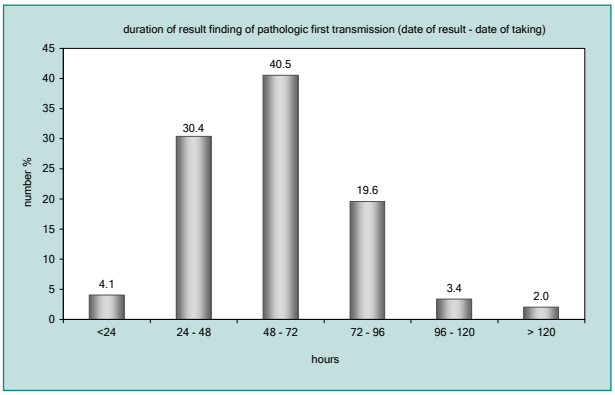

Fig. 4

The result which is shown by figure 3 reflects also the transmission time of pathological results (in total 148).

Figure 4 shows that in 3 cases the result determination needed more than 5 days.

Diagnostics Time of All Results

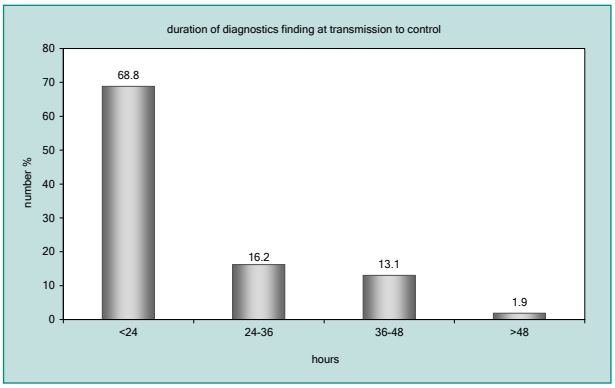

Fig. 5

The diagnostics time is influenced by factors like internal repetitions (necessary, if the first result is classified as pathological) and malfunction of devices.

98.1% of all results (2010: 98.1%) were determined and transmitted within 48 hours (the printing date counts at normal results and the date of oral transmission at results which need to be controlled again. The time is documented here on the data set of the infant.)

Diagnostics Time of Pathological Results

Figure 6 shows the distribution of the diagnostics time of the first transmissions with pathological result. All results were present after less than 72 hours. In 2010 two results were not present before 72 hours after transmission due to a missing declaration of agreement.

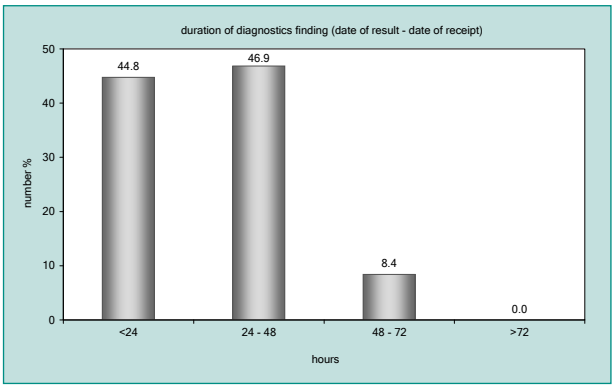

Fig. 6

The following figure 7 shows the time period from oral transmission of the 141 results up to the income of the sample to control. Generally, pathological results are transmitted orally and faxed as partial result after they were confirmed internally by the laboratory. All these activities are documented.

In nine cases with a response time of more than 120 hours premature infants were concerned. In these cases, the taking of the sample to control was postponed to a gestational age of 32 weeks (timely second blood taking).

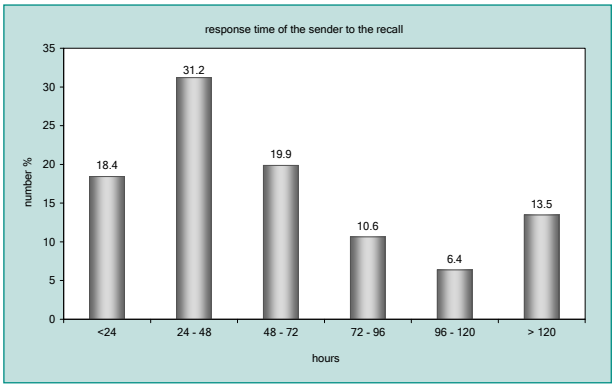

Fig. 7

10 suspicious screening cases were confirmed by confirmation diagnostics. Four children suffered from a hypothyreosis, four children suffered from a phenylketonuria/ hyperphenylalaninemia (HPA), one infant suffered from disorders in metabolising middle-chain fatty acids (MCAD) and one infant had a complete biotinidase deficiency.

Therapy Starting at Patients with Positive Screening

Nine infants needed a therapy:

Tab. 5: Diagnosis, confirmation diagnostics and therapy starting

Diagnosis	Confirmation diagnostics	Age at start of therpy
4 x Hypothyroidism	Serum-TSH, T4, sonography	5-8 days
3 x Phenylketonuria	Serum-Phe, BH4-test	11-15 days
1 x Biotinidase deficiency	Biotinidase activity in serum	9 days
1 x LCHAD deficiency	mutation analytics	6 days

One child which suffered from HPA does not need a therapy.

Summary

Similar to the previous year no changes took place in the specifications of the Federal Joint Committee of physicians and health insurances (G-BA). However, in March 2011 the Children Directive was adjusted to the Gene Diagnostics Act and several modifications in regard to the newborn screening came into effect.

Thereby, the Gene Diagnostics Act still is and remains the superordinated act with its own paragraphs of penalty. The modifications of the Children Directive are mainly referring to exceptions in special cases. One update for example is that midwifes can also give the relevant information about the screening when it is assured that a physician can be contacted at any time for further questions. According to the new Directive, the time for consideration can be forgone and blood withdrawal can take place immediately after consultation with the physician. It is also an improvement that the the agreement on hand for the laboratory can be confirmed only with a mark in the corresponding field on the filter paper card. If a nomination is exceptionally not possible, the midwife has to carry out the screening on her own responsibility - also a new rule. In case of a pathological result, this result has to be transmitted immediately from the laboratory consultant to the sender (new: also to the midwife) in oral and written form.

The transmission times (figure 1-7) could not be improved in 2011. Possible reasons might be outer conditions such as the delivery services.

All patients with a positive first screening result were followed up and their diagnosis was assured resp. excluded. The confirmation of the positive screening result by the attending medical institution and the start of a therapy were documented in all cases.

We calculated an incidence of 1/1666 for all objective diseases of the newborn screening in Saxony-Anhalt in 2011.

For further information about the metabolic screening centre Magdeburg we kindly invite you to visit our website:

www.stoffwechselzentrum-magdeburg.de

We would like to inform sender, parents and interested people here about the Newborn Screening and the Newborn Hearing Screening and provide downloads. We update our website on a regular basis.