REVIEW ARTICLE

Treatment of Preterm Infants at the Lower Margin of Viability – a Comparison of Guidelines in German Speaking Countries

Roland Hentschel, Stella Reiter-Theil

SUMMARY

Introduction: The treatment of preterm infants at the lower margin of viability is carried out amid growing tension between increasing survival rates, uncertain clinical outcomes, and financial and ethical considerations. The three German speaking countries have released guidelines on this issue, based on a previous common guideline. That is why the differences in national guidelines between the three countries is of peculiar interest in respect of medical ethics.

Methods: Current guidelines from Germany, Switzerland, and Austria were compared and similarities and differences discussed.

Results: The three countries' guidelines follow broadly similar principles, with almost identical intellectual underpinnings and formulations. Some national differences are apparent, nevertheless.

Discussion: All three guidelines call for a pragmatic approach. National guidelines can only predetermine the framework, with long-term collection of sound local data on morbidity and mortality forming a prerequisite for decision-making, and also in discussions with parents.

Dtsch Arztebl Int 2008; 105(3): 47–52
DOI: 10.3238/arztebl.2008.0047

Key words: preterm infant, viability, palliative care, ethics, guidelines

A growing number of guidelines in different medical specialties is intended to promote standardized procedures with due consideration of scientific insights. Even medical decisions with ethical implications are increasingly discussed in national guidelines. In neonatology, the question from which week of gestation preterm infants should receive consistent life saving care is at the center of intense national and international debates (*box 1*) (1–4). What is known is that as far as this question is concerned, it is not only fundamental attitudes but actual procedures that vary among neonatologists in different European countries (5). Systematic comparative studies of different national guidelines with a medicoethical background are few and far between (6–8).

The authors used three current national guidelines (Germany, 1999; Switzerland, 2002; Austria, 2005) to compare commonalities and differences between countries with regard to the treatment of preterm infants at the lower margin of viability (9–11).

On the basis of an originally common guideline, the three German speaking countries have issued their own guidelines on this subject in recent years. For this reason, these guidelines are of particular interest for an analysis of national differences with regard to medicoethical considerations.

Guidelines: origins, structure, and system

The first guideline on treating extremely preterm infants was set out in the name of the joint scientific neonatology society of the German speaking countries (GNPI, the Society for Neonatology and Pediatric Intensive Care [Gesellschaft für Neonatologie und Pädiatrische Intensivmedizin]) under the aegis of F. Pohlandt in Ulm and published in 1999. The guideline was based on a survey among the 21 biggest neonatology departments in Germany and collected data on their 1995 to 1997 death rates in preterm infants of less than 27 weeks' gestation. In 2000, neonatologists in Switzerland already set out their own recommendations (the current version dates from 2002), and in 2005, Austria's guidelines were published. The first GNPI guideline by Pohlandt can therefore with some justification be referred to as the "German guideline," since it is now applied only in Germany. All three

Funktionsbereich Neonatologie und Intensivmedizin, Zentrum für Kinder- und Jugendmedizin, Universität Freiburg: PD Dr. med. Hentschel

Institut für Angewandte Ethik und Medizinethik, Medizinische Fakultät der Universität Basel, Schweiz: Prof. Dr. rer. soc. Reiter-Theil

BOX 1

Main issues addressed in the guidelines of other countries

Sweden (guideline of 2004) (19)

- Centralized care
- Individual action between 23 and 25 weeks' gestation
- Obtain parental consent

USA (guideline from 2002) (20)

- <23 weeks' gestation or <400 g birth weight
Do not resuscitate!
- No regulation for higher gestational ages

Australia (guideline from 2006) (16)

- Increasing obligation to treat between 23 + 0/7 weeks' gestation and 25 + 6/7 week's gestation
- Exception to be made if parental consent refused after appropriate advice/counseling

BOX 2

Content and structure of the guidelines

Germany

- Before 22 weeks' gestation
- 22 to 23 + 6 weeks' gestation
- 24 weeks' gestation and later
- Preterm infants with congenital and perinatally acquired health problems

Switzerland

- Ethical aspects
- Communication
- Antenatal recommendations
- Postnatal recommendations
- Decisions on the neonatal intensive care unit
- Recommendations for quality assurance

Austria

- Legal aspects
- Ethical aspects
- Medical aspects
- Recommendations

guidelines are supported by thematically "neighboring" scientific societies or working groups. In Germany, these are the societies for perinatal medicine, for gynecology and obstetrics, for pediatrics and adolescent medicine, and the GNPI; the cooperation of moral theologians and criminal law experts also deserves a mention. In Switzerland, support comes from the societies for gynecology, pediatrics, and neonatology as well as the central ethics committee of the Swiss Academy of Medical Sciences (SAMS). In Austria, the working group for neonatology and pediatric intensive care, as well as the working group for ethics of

the Austrian Society of Pediatrics and Adolescent Medicine are partners.

The contents, extent, and emphasis of the guidelines are reflected by the chapter headings (*box 2*). All three guidelines provide essential background information on morbidity and mortality data and on the importance of gestational age and the biological variability of the neonate. Further, they include a bibliography (for the Austrian guidelines, this is available only online). The two more recent guidelines – Austria's and Switzerland's – are more detailed, give more space to ethical aspects, and take an explicit position with regard to ethics.

Comparative analysis

What is the basis of the guideline?

Guidelines can justify the ethical and normative statements they contain by referring to different sources: principles of medical ethics, general value systems, legal parameters, e.g., from criminal law, but also principles of action from medical self-governance.

In the German guidelines, reference is made repeatedly in a general way to "ethical and legal standards." Both the other guidelines have separate sections on "ethical considerations" (Switzerland) and "ethical aspects" (Austria).

The Austrian guideline is the only one to provide an overview over legal aspects. In none of the three countries, however, is there a special legal regulation of how to proceed with regard to treatment or limiting treatment in extremely preterm infants. They still all refer to legal categories. Important categories in the fundamental orientation of the guidelines are obvious in the way that the question of saving lives is dealt with. The German guideline states: "Life saving measures will have to be taken if the infant has any chance of survival, however small." Austria's guideline also acknowledges the right to life from birth that is granted in the country's constitution and emphasizes the principle "in case of doubt, favor life." The Swiss guideline, by contrast, emphasizes that the prospects of the infant of an "acceptable quality of life" should be considered, as should the question of whether "the current therapies are tolerable," and they warn of overtreatment. Economic considerations are not part of any of these guidelines; they should generally be considered but not play a part in the individual case scenario (Switzerland and Austria).

Who should make decisions?

All three guidelines include doctors, midwives, nursing staff, and other professional groups, as well as the parents, in their deliberations. The Swiss guideline clarifies on various occasions that the parents "together with the responsible medical staff" should make decisions. They state that a decision on behalf of the baby is needed, and they include society itself as a responsible party, in the sense of an ethics committee or a court of law. All guidelines leave open, however, with whom the priority should lie or how to proceed in

TABLE 1

Categorization by gestational week

	Germany	Switzerland	Austria
22 + 0/7 to 23 + 6/7	Indifferent, mention sequelae, consider "parental interests"	"As a rule, palliative measures" ("comfort care")	If vital functioning is good, "provisional care"
24 + 0/7 to 24 + 6/7	Always support vital functions; "right to life" is given	"Decision in the delivery room"; "provisional care"; caesarean section for the sake of the fetus rarely indicated	Tocolysis, lung maturation; as a rule: give intensive care; individual decision on caesarean section
From 25 + 0/7	See above	See above and caesarean section indicated	Caesarean section indicated

case of a disagreement. Only the Austrian guideline states regarding this important issue that in a case of doubt (this means if even only one person gives a positive vote), treatment should be administered or continued, so that an unanimous vote is required in order to not treat or stop treatment. This corresponds to the fundamental principle of reaching decisions whose outcomes are irreversible only by consensus (12, 13). With reference to patient safety, it is stated that far-reaching decisions should not be made by individuals but by a "multidisciplinary team ... and by including and taking into consideration the interests and wishes of the parents."

The German and Swiss recommendations point at a potential conflict arising from the general medical duty to save life. The German guidelines say that "doctors as guarantors for the child may have to ... act against the parents' wishes if the occasion requires it."

The parents' role

The parents have to be included in advice, information, and the search for consensus, according to all three guidelines. None of the three texts, however, regards the parents as independently or exclusively competent decision makers in the sense of a legally and ethically legitimate representative of the child, but they are regarded as people in need of protection, who should primarily be protected from the burden of an irreversible decision. Accordingly, the German guideline sees its recommendations as an aid for parents in making "ethical and legally based decisions." The parents' scope for decision in the "start and end of life-saving measures for their unborn and born child" – which should already be pointed out in the antenatal advice session – is the subject. The central ethical and legal statement is that the parents should separate their own interests from those of the child and are obliged to giving priority to the child's best interests.

The Swiss guideline is more detailed on this topic and prioritizes among legal aspects doctors' duty to provide information and elucidation. The Austrian guideline makes its subject the entire family in addition to the parents, whose individual members may be badly affected by mortality and long-term morbidity

of the preterm neonate. With regard to legal aspects, it limits the parents' scope for decision and demands putting personal deliberations behind the protection of human life. The priority in all three guidelines lies with those administering treatment and provides for obtaining consent from the parents. This constellation is not critically reflected in any of the three guidelines, even if in practice there may be situations where the parents may have good reasons for deviating from the recommendation. According to this state of affairs – and if the maxim "if in doubt, favor life" is adhered to – this would mean in a conflict scenario that parents cannot effect a stop to treatment or demand refraining from treatment altogether if the team does not agree. The Swiss guideline mentions involving a court of law in case of escalation. Targeted ethical advice to prevent conflict is not mentioned in any of the guidelines, although ethics councils are common in pediatrics in many places (14).

Prenatal stratification and indication for caesarean section

All three guidelines recommend an (early) transfer to a perinatal center at different stages of gestation, and involving a neonatologist in the care even before birth. Further active measures – e.g., tocolysis, prophylaxis with corticoids, or cesarean section for a pediatric indication – is stratified by completed week of gestation (*table 1*).

According to the Swiss guidelines, the event of an in-utero transfer to a perinatal center, as well as particularly the event of a cesarean section, does not necessarily entail the need for active postnatal proceedings. The guidelines regard caesarean section as a risk factor for the pregnant woman and give a clear indication only after 25 + 0/7 weeks' gestation. In reverse, the current care strategy (prenatal fetal lung maturation) may have a positive effect on consistent medical care after the birth.

For Austria and Switzerland, the time period 24 + 0/7 to 24 + 6/7 weeks' gestation is a grey area with regard to obstetric emergency measures. It is implied that a caesarean section for a maternal indication may be done earlier than that. The counter-argument is that this potentially worsens the chances of the unborn child, which touches on the ethical principle of

TABLE 2

Mortality and morbidity of extremely small preterm infants (16)

	23 + 0/7 to 23 + 6/7 weeks* ¹	24 + 0/7 to 24 + 6/7 weeks* ¹	25 + 0/7 to 25 + 6/7 weeks* ¹
Alive at discharge* ²	29%	50%	65%
Severe retinopathy	64%	27%	15%
Severe cerebral hemorrhage or parenchymal cysts	7%	14%	11%
No functional impairment* ³	33%	61%	67%
Severe functional impairment* ⁴	33%	19%	13%

*¹gestational age;

*² Admitted to intensive care, in percent

*³, *⁴ Examined at age 3 with Griffith Mental Development Scales; Bayley Scales of Infant Development, in percent;

*³ Developmental quotient above minus 1 standard deviation from the reference cohort;

*⁴ Developmental quotient below minus 3 standard deviation from the reference cohort

+/- bilateral blindness/high-grade visual impairment +/- cerebral paresis;

This is one of the largest, current, population-based studies, including 897 preterm infants at less than 26 weeks' gestation of birth years 1998 to 2000 in two Australian regions.

avoiding any harm to the fetus (15). The German guideline does not take position with regard to prenatal management and indication for caesarean section depending on the gestational age.

Inclusion of statistical data

The current guidelines base their recommendations on mortality and morbidity data and demand systematic long-term data and investigations into the prognostic importance of vital functioning at birth, in order to better support decisions to be made in the future. The German and Swiss guidelines take into consideration national data on the mortality of extremely small preterm infants, but for the important question of long-term morbidity they cite international studies, owing to a dearth of solid national data. Only the Austrian guideline refers to national Austrian mortality and morbidity data. All three guidelines stress that local statistics should be known, for decision making purposes as well as for communicating with the parents. Table 2 summarizes current mortality and morbidity data (16). The German guideline will be updated in the not too distant future and will include more recent national data on mortality and preterm morbidity (1).

According to the Swiss and Austrian guidelines, a multiprofessional team should be making advance decisions on the care strategy of extremely preterm infants. The process of establishing local guidelines in such a way has recently been described in an exemplary fashion (17).

Limitations and imponderabilities

Decisions and considerations made before birth will become obsolete if the preterm infant is either more viable or much less viable than expected. All three guidelines mention the imponderabilities that arise because of the discrepancy between the prenatally determined gestational age and the extent of somatic maturity that is ascertained after birth. In addition, preterm infants of the exact same (and correctly deter-

mined) maturity can have very different Apgar scores ("biological variability"). The Swiss and Austrian guidelines state that in such scenarios, the predetermined way of proceeding may have to be reviewed. According to the Austrian guidelines, postnatal viability is more important than measured gestational age, but further studies into long-term outcomes are needed. Biological variability with its potentially significantly different overall prognosis has been shown for the comparison between equally mature preterm infants in relation to sex, ethnic origin, normal versus inadequate intrauterine growth (intrauterine hypotrophy), and singleton or twin status (17, 18). But other unknown or already known factors – e.g., the extent of intrauterine fetal stress, underlying pathologies such as intrauterine infections, and the care strategy applied thus far (fetal lung maturation) – can have an important role in prognosis and the decision making process, but are not mentioned in the guidelines.

This means that an orientation by gestational age measured in weeks can be questioned, not only because of uncertainties in the exact determination of the duration of pregnancy.

Care strategy, changing therapeutic goals, and limiting curative treatment

All three guidelines give a limit above which intensive medical treatment of the preterm infant should be given; in the German and Austrian guidelines, this threshold is 24 + 0/7 weeks' gestation, in the Swiss guideline, 25 + 0/7 weeks. All three guidelines agree that the scope for an individual decision according to the current situation will have to be wide. For the treatment of neonates below the stated limit, the Austrian guideline recommends "provisional intensive care," in case the acute situation shows up some pointers to unusually good vital functioning in a preterm neonate of less than 24 + 0/7 weeks' gestation.

The important topic of switching from curative to palliative care, or the primary application of palliative

TABLE 3

Important differences between the guidelines

	Germany	Switzerland	Austria
Main criterion	Gestational age limit < / = or > 23 + 6/7 weeks' gestation	Strict orientation on gestational age, but depending on postpartum vital functioning exceptions can be made	Stratification by "provisional care" versus "comfort care", independently of gestational age
Particularities	Based on old data (mortality statistics); from 24 + 0 weeks' gestation "right to life", independent of grade of maturity, "if necessary, against the parents' wishes"	Prenatal fixing by transfer strategy (perinatal center); emphasis on parental wishes and communication with parents	Unanimous decision required; strong emphasis on postpartum vital functioning

care, is addressed in all three guidelines, and even described in some detail. The guidelines recommend administering opiates in almost the same terms, even at the price of possibly shortening the infant's life; the idea of using opiates to kill the patient is explicitly rejected, however. Supportive measures in the sense of "comfort care" are listed, as is the inevitable inclusion of the parents in the dying process of their baby.

The Austrian guideline anchors the therapeutic change towards palliative care on the following: „a poor prognosis in terms of a life lived with human dignity,“ and „a patient who is very close to death – i.e., dying.“ The Swiss guideline weighs up „a potential future gain against the suffering inflicted by the treatment.“ The defined therapeutic aim is that the child should survive „with an acceptable quality of life.“ None of the cited terms is more closely defined.

Reasons for limiting therapy in the German guideline are deducted from the (statistically) evident hopelessness with regard to survival or from the likelihood of lasting disabilities or impairments in preterm infants with a gestational age of less than 24 completed weeks. The Swiss guideline provides the most closely circumscribed stratification. According to the Austrian guideline, the individual development, independent of gestational age, and a weighing up of the overall prognosis (including the likelihood of lasting impairments) should be consulted.

Only the German guideline refers briefly to preterm infants and neonates who (additionally) have malformations or concomitant serious disorders that make survival or a life without severe lasting impairment seem impossible – a situation that occurs more often than mere prematurity at the lower margin of viability (12).

Conclusion

All three guidelines base their recommendations on the care of preterm infants at the lower margin of viability on the same principles – in some places, the phrases and arguments are as good as identical. But their implementation leads to different conclusions. National differences are obvious – e.g., in the emphasis on "postpartum vital functioning" in Austria or the pragmatic orientation on gestational age groups in

Switzerland (table 3). But in all three guidelines, it is clear how difficult it is to balance a pragmatic guideline recommendation, oriented by gestational age groups, and the necessity to take into consideration the patient and patient's family with all their individual circumstances. If a more stringent admission of high-risk patients to the most qualified specialized centers in the country is intended then that is exactly where the necessary expertise for medico-ethical counseling should reside. In future, it should be obligatory for long-term data on the residual morbidity of former preterm infants (e.g., at the age of 2) to be included in the evaluation of the neonatal data collection, with which the individual perinatal centers will have to compare their own results. Proceeding in such a way should result in a better basis for decision making and to counsel the parents (box 3).

Conflict of interest statement

The authors declare that no conflict of interest exists according to the guidelines of the International Committee of Medical Journal Editors.

Manuscript received on 29 March 2007; revised version accepted on 13 August 2007.

Translated from the original German from Dr. Birte Twisselmann.

REFERENCES

- Herber-Jonat S, Schulze A, Kribs A et al.: Survival and major neonatal complications in infants born between 22 0/7 and 24 6/7 weeks of gestation (1999–2003). *Am J Obstet Gynecol* 2006; 195: 16–22.
- Fauchère JC, Bucher HU, Moriette G et al.: Survival and major neonatal complications in infants born between 22 0/7 and 24 6/7 weeks of gestation (1999–2003). *Am J Obstet Gynecol* 2007; 196: e60.
- Herber-Jonat S, Pohlandt F, Schulze A: Reply. *Am J Obstet Gynecol* 2007; 196: 60–1.
- Genzel-Boroviczény O, Friese K: Frühgeborene an der Grenze der Lebensfähigkeit. *Dtsch Arztebl* 2006; 103(28–29): A 1961–4.
- Cuttini M et al. for the EURONIC study group: End-of-life decisions in neonatal intensive care: physicians self-reported practices in 7 European countries. *Lancet* 2000; 355: 2112–8.
- Bartels S, Parker M, Hope T, Reiter-Theil S: Geben „Richtlinien“ bei kritischen Therapieentscheidungen ethische Orientierung? Eine vergleichende kasuistische Analyse der deutschen Grundsätze, britischen Guidelines und schweizerischen Richtlinien zur Sterbebegleitung. *Ethik Med* 2005; 17: 191–205.
- Dalla-Vorgia P, Mason SA, Megone C et al. on behalf of the Euricon Study Group: Obtaining informed consent for neonatal research. *Arch Dis Child Fetal Neonatal Ed* 2001; 84: 70–3.
- Mason SA, Allmark PJ, Megone C et al. for the Project Management Group: Obtaining informed consent to neonatal randomized controlled

BOX 3

Development of former preterm infants

Some 1300 preterm infants at the lower margin of viability (less than 26 weeks' gestation) are born in Germany each year. Data on mortality and early morbidities (cerebral hemorrhages, retinopathies, chronic lung diseases) are known from the neonatal data collections of the individual federal states, which work with a common dataset; but no national statistics exist. Also, no reliable data are available at the state level with regard to the long-term morbidity of these patients, although this is enormously desirable, in order to facilitate objective discussion about ethical or medical limitations at the lower margin of viability. A decision of the federal joint committee (GBA [Gemeinsamer Bundesausschuss], the supreme decision-making body in the joint self-governance of doctors, dentists, psychotherapists, hospitals, and health insurance companies in Germany) demands from year of birth 2006 a standardized follow-up examination at the age of 2 years, with a capture rate of at least 80% per perinatal center. It is not clear thus far whether these long term data will be included in the neonatal data collection, whose new edition is currently under discussion under the aegis of the BQS (the federal body for quality assurance). Larger Angloamerican studies (mostly monocenter or multicenter studies) contain reliable long-term data documenting the development of previously very small preterm infants to adulthood; obviously, their results reflect neonatology at the end of the 1980s. Larger population-based studies come from the United Kingdom and Australia, among others. Individual German states have results on mortality and early morbidity that are in no way inferior to the published data of the best international studies. A worldwide registry (Vermont Oxford Network, a non-profit voluntary collaboration of healthcare professionals dedicated to improving the quality and safety of medical care for neonates and their families) currently captures 45 000 preterm births of infants of less than 1500 g birth weight from more than 700 participating hospitals worldwide and evaluates these scientifically.

trials: interviews with parents and clinicians in the Euricon Study. *Lancet* 2000; 356: 2045–51.

9. AWMF online – Frühgeburt an der Grenze der Lebensfähigkeit des Kindes. Leitlinie Nr. 024/019 (1999). www.awmf.de
10. Schweizerische Leitlinie: Arbeitsgruppe der schweizerischen Gesellschaft für Neonatologie – Empfehlungen zur Betreuung von Frühgeborenen an der Grenze der Lebensfähigkeit. *SÄZ* 2002; 83: 1598–5.

11. Österreichische Leitlinie: Österreichische Gesellschaft für Kinder- und Jugendheilkunde – Erstversorgung von Frühgeborenen an der Grenze der Lebensfähigkeit; *Monatsschrift Kinderheilkunde* 2005; 7: 711–5.
12. Hentschel R, Lindner K, Krüger M, Reiter-Theil S: Restrictions of ongoing intensive care (RIC) in neonates – a prospective study. *Pediatrics* 2006; 118: 563–9.
13. Reiter-Theil S, Hentschel R, Lindner K: Lebenserhaltung und Sterbegleitung in der Neonatologie. Eine empirische Ethik-Studie zu kritischen Therapieentscheidungen. *Zeitschrift für Palliativmedizin* 2005; 6: 11–9.
14. Reiter-Theil S: Klinische Ethikkonsultation – eine methodische Orientierung zur ethischen Beratung am Krankenbett. *Schweizerische Ärztezeitung* 2005; 86: 346–52.
15. Beauchamp TL, Childress JF: *Principles of Medical Ethics*. New York: Oxford University Press 1994.
16. Lui K, Bajuk B, Foster K et al.: Consensus Statement – Perinatal care at the borderlines of viability: a consensus statement based on a NSW and ACT consensus workshop. *Med J Aust* 2006; 185: 495–500.
17. Kaempf JW, Tomlinson M, Arduza C et al.: Medical staff guidelines for periviable pregnancy counselling and medical treatment of extremely premature infants. *Pediatrics* 2006; 117: 22–9.
18. Phelbs DL, Brown DR, Tung B et al.: 28-day survival rates of 6676 neonates with birth weights of 1250 grams or less. *Pediatrics* 1991; 87: 7–17.
19. Peerzada JM, Schollin J, Håkansson S: Delivery room decision-making for extremely preterm infants in Sweden. *Pediatrics* 2006; 117: 1988–95.
20. MacDonald H and Committee on Fetus and Newborn: Perinatal care at the threshold of viability. *Pediatrics* 2002; 110: 1024–7.

Corresponding author

PD Dr. med. Roland Hentschel
Funktionsbereich Neonatologie und Intensivmedizin
Zentrum für Kinder- und Jugendmedizin
Universität Freiburg
Mathildenstr. 1
79106 Freiburg, Germany
roland.hentschel@uniklinik-freiburg.de