

Conference report

Public health and prevention of congenital anomalies

*Fifth European Symposium on the Prevention of Congenital Anomalies, 8 May 1996,
Groningen, the Netherlands*

1. Introduction

Two to three percent of all infants are born with a major congenital anomaly. Often these children are born to parents who did not have any known increase in risk for bearing children with such anomalies. In recent decades the possibilities for primary prevention and for intervention after prenatal diagnosis have increased. Different countries have developed divergent policies in this respect, and this Symposium set out to discuss the basis for making such a choice and the potential effects of policy. Epidemiologists working in the field of congenital anomalies, clinical geneticists, obstetricians involved in prenatal diagnosis, and health policy makers were all involved.

Prominent topics at the Symposium included Down's syndrome, the influence of ultrasound, and the role of vitamins; striking was the fact that alongside the purely scientific issues so much attention was devoted to resolving the ethical and political issues which arise where congenital defects are concerned.

In association with the Symposium there was an annual meeting of registry leaders of the EUROCAT-network ("European Registration of Congenital Anomalies").¹ EUROCAT is a network of 30 registries in 16 countries, mainly within the European Union, which aims to collect information on congenital anomalies since 1979. Details of EUROCAT, and the texts of papers and posters from the Symposium are available from EUROCAT-registration, Ant. Deusinglaan 4, NL-9713 AW Groningen.

What follows here is a brief report of some highlights of the Symposium; they comprise a paper by two representatives of the Netherlands parents' organisation for Down's syndrome, another by Prof. E. Borst-Eilers, Minister of Public Health, Welfare and Sports, the Netherlands, and a summary of the general discussion.

M.C. Cornel
Groningen
The Netherlands

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¹The local scientific committee comprised Dr J.R. Beekhuis, obstetrician, University Hospital Groningen, Department of Obstetrics and Gynaecology; Dr M.C. Cornel, epidemiologist, University of Groningen, Department of Medical Genetics; Dr L.T.W. de Jong-van den Berg, pharmacist, University of Groningen, Department of Social Pharmacy and Pharmacoepidemiology; and M.B. Tan-Sindhunata, clinical geneticist, Free University of Amsterdam, Department of Human Genetics. Sponsors were the firms Pharmachemie and Abbott Diagnostics and the Foundation for Genetic Information (Stichting voor Erfelijkheidsvoorlichting) Groningen.

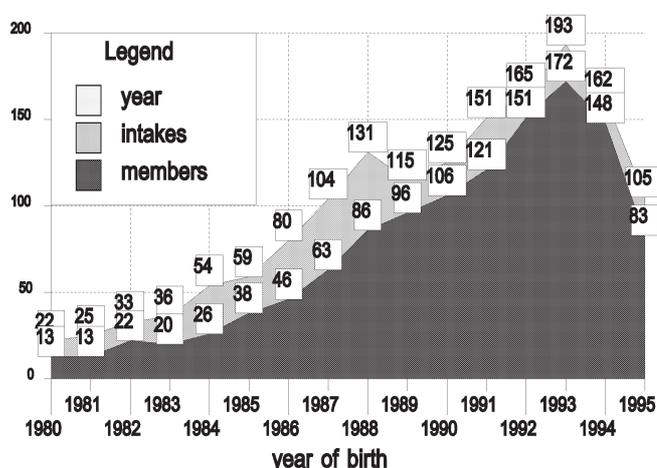


Fig. 1. Membership of the Netherlands Down's Syndrome Foundation, according to the dates of birth of the children concerned.

2. The future of Down's syndrome: a plea for more- and more realistic-options

E.A.B. de Graaf and M. de Graaf-Posthumus

Stichting Down's Syndrome (SDS), Wanneperveen, the Netherlands

At a rough estimate, some 200 babies with Down's syndrome are born in the Netherlands every year [1]. No accurate calculation of the total incidence of the syndrome is possible, since recent data on the termination of pregnancies in the Netherlands are lacking. Large academic centres have neither been able to determine the numbers of pre-natal diagnoses carried out over time, nor have they been able to record figures on their follow-up.

In 1988 the Dutch Down's Syndrome Foundation (Stichting Down's Syndroom, or SDS for short) came into being. Its goals can be summarised under the three headings: *information, intervention and integration*. As such, one of the priorities of the SDS is to provide support to 'new' parents whose offspring display the syndrome. From the start, every effort has been made to reach as many parents as possible, as soon as possible after the diagnosis has been made or the child has been born. Increasing proportions of parents of successive birth cohorts have consulted the SDS (Fig. 1). Using the available information, it can be calculated that in 1993, for example, the parents of some 90% of all babies with Down's syndrome born in that year indeed contacted the Foundation. In recent years, such contact has been established earlier than in the past; the 75th percentile of the average age at intake decreased from 19 months in 1988 to 5 months in 1995. As of 1996, the SDS had almost 2000 families with one or more children with the condition on its files.

Despite the existence of this apparently very successful syndrome-specific organisation, Down's syndrome is in the Netherlands usually regarded by the population at large as a very serious problem – so much so that the great majority of pregnancies in which a foetus with Down's syndrome has been identified are still terminated. Data for 1989 from the annual review of the working party on prenatal diagnosis of the Dutch Association for Obstetrics and Gynaecology and the Association for Clinical Genetics, suggest that 50% of the mothers in whom prenatal diagnostic testing is indicated actually made use of it; the corresponding figure for 1990 appears to have been 56% [2]. In the absence of more recent figures, one has the impression that the number of live births with Down's syndrome has been falling; additional support for this view comes from the decreasing number of intakes at the SDS after 1993

(Fig. 1). Eurocat Groningen, similarly, has stated that a considerably lower number of live births with Down's syndrome was reported over 1994 [3]. One may also note that only seven out of some 2000 couples in the SDS-inventory knew their child's diagnosis beforehand, and in only five of these cases was the prenatal diagnosis carried out intentionally. The parents concerned recalled that their decision to allow the pregnancies to go to term met with very little understanding, suggesting that health professionals regarded their choice as an exceptional one.

2.1. *The a priori position*

Over the years, termination of pregnancies showing a foetus with Down's syndrome has thus emerged as the widely accepted "first choice" option. Underlying this view is the widely held *a priori* position that "Down's syndrome is a severe handicap which necessarily leads to unbearable suffering for both children and their families". This then leads on to some apparent consensus that *a child with Down's syndrome should not be born at all*.

In a recent study, carried out at the request of the Netherlands Secretary of State for Health, a number of scenarios were developed for prenatal diagnosis and its follow-up was examined. The results were presented in such a manner as to suggest that this *a priori* position reflected a universal consensus, no further discussion of which was justified [4]. In our view, a Secretary of State who sets out to develop health policies on the basis of studies such as these is building on a very uncertain foundation; this is particularly the case when one bears in mind the lack of accurate and recent data on prenatal diagnosis and its follow-up.

2.2. *The position of the SDS*

The Foundation supports freedom of choice *for the parents-to-be* where a prenatal diagnosis has delivered a positive outcome. It rejects the view that *society as a whole* can validly act as the body to determine (for example, through policy guidelines) whether pregnancies in which the outcome of prenatal testing has been positive should be terminated. In the view of the SDS any child should feel that it is welcome in society; whether or not the parents have purposely chosen to let him or her be born, should make no difference at all. Furthermore, the SDS believes that for individual parents a sound judgement as regards termination or otherwise is only possible – and even then extremely difficult – on the basis of high quality, up-to-date information. In actual practice the situation, at least in our country, leaves much to be desired in this respect. Very many of the professionals with whom parents in this situation come into contact are motivated by obsolete information and attitudes. In fact it would appear that many of them have never have seen a child with Down's syndrome at close range, nor are they aware of the possibilities open to such a child at the present day. Parents often quote highly improper statements from professionals. The second author of this paper heard a gynaecologist declare at a recent symposium on prenatal diagnosis in the Netherlands: "I cannot guarantee parents what they are going to get: a funny, well-functioning mongol or an aggressive rascal". Parents counselled by a profession holding such opinions will be more prone to accept the *a priori* view than will parents who have thoroughly investigated recent information on the syndrome [5].

2.3. *The a priori position put to the test*

A recent Dutch study examined the health-related quality of life (HRQOL) of as large a population as possible of children with Down's syndrome. HRQOL was defined as health status plus affective responses to problems in health status. With a response rate of 77%, 741 respondents were available for

study. The results showed that, in the parents' view, only 5% of children experiencing problems in motor, role or cognitive functioning felt badly about themselves as a result of such problems. It has been suggested that HRQOL essentially reflects about how people feel about their own functioning, i.e., it is about affective responses and not the actual state of health. Judged by this standard, the health-related quality of life of most children with Down's syndrome was, in the view of these investigators, excellent [6,7].

One point sometimes advanced emphatically in support of the *a priori* position is the high cost of institutionalization, as assessed using cost-benefit analyses. This approach is largely irrelevant: at the present day, the children concerned are seldom institutionalized. In the eight years since SDS was founded, we have not recorded a single case of institutionalisation on the Foundation's files.

2.4. *The problem is the syndrome and not the child*

For the greater majority of parents within the SDS, the problem is the *syndrome* and not the *child* [5]. The distinction is a very fundamental one. Awareness of it can lead to a totally different and more enlightened approach to Down's syndrome for the future.

Firstly, as far as the channelling of research money is concerned, top-priority should surely be accorded to finding means of primary prevention, analogous to the use of folic acid supplementation in the case of spina bifida. This would supplant the current obsession with developing ever more refined prenatal diagnosis, inevitably leading in many cases to termination.

For the remaining pregnancies in which a risk factor has been identified, early prenatal diagnosis having a positive outcome should always be followed by a thorough and up-to-date review of what Down's syndrome means. In this process, the involvement and support of syndrome-specific organisations, such as SDS, is vital.

Where the outcome of prenatal diagnosis is positive, parents should be offered adequate help in considering the following three options, in this order: (a) carrying the pregnancy to term, to be followed by the best possible upbringing (b) ditto, with the aid of a biochemical intervention to suppress the development of the characteristics of Down's syndrome and finally (c) termination of the pregnancy.

Several additional comments on this proposed approach seem justified.

Firstly, parents knowing in advance that they will never opt for termination of pregnancy would perhaps be wise not to seek prenatal diagnosis at all; it will not be of use to them, and so long as biochemical testing is not sufficient it will involve a degree of risk.

Secondly, parents deciding to continue pregnancy after a positive outcome of prenatal diagnosis should never be pressured to change their minds; on the contrary, they should be offered all necessary support. At present this leaves much to be desired, at least in the Netherlands.

Thirdly, it must be realised that while biochemical intervention to prevent Down's syndrome is still in the future, it is certainly no more remote than is medication for Alzheimer's disease or AIDS, at least if the choice is made to undertake adequate research effort in the field. Recent work by Busciglio and Yankner indicates where such work may lead. They compared cortical neurones from foetuses with Down's syndrome with those of age-matched foetuses without the condition [8]. Initially, both types of neurones appeared to differentiate normally in culture. However, subsequently, the Down's syndrome neurones degenerated and underwent apoptosis, whereas the normal neurones remained viable. Degeneration of the Down's syndrome neurones could be prevented by treatment with anti-oxidants. Furthermore, Down's syndrome neurones exhibited a three to fourfold increase in intracellular *reactive oxygen species* (ROS), in conjunction with elevated levels of lipid peroxidation, preceding neuronal death. These results suggest that Down's syndrome neurones have a different metabolism of ROS that causes apoptosis. It is

thought that the increased amounts of ROS could contribute to the abnormal development of the brain, and thereby the mental retardation seen in Down's syndrome. Where this happens, neuronal depletion and structural abnormalities may become evident during later gestational stages of brain development and early in post-natal life [8]. In actual fact, the suggestion of using anti-oxidants to alleviate symptoms is nothing new. The present authors heard it advanced by Lejeune, the discoverer of the trisomy 21, in Brighton in 1986 [9].

The costs of extensive research into the prospects for biochemical intervention might usefully be compared in broad terms with those incurred in prenatal diagnosis. According to Elkins [10], the costs of undertaking a full triple screen wherever indicated, followed by ultrasound and amniocentesis where necessary, amount to some \$190,000 for every case of Down's syndrome identified. Financing this is the one scenario. This cost of \$190,000 per foetus with Down's syndrome could, in principle, be put to a totally different use. The same amount of money could be used to pay the salaries of at least two high-level researchers for one year. In this manner, rather than directing investment primarily to the detection of foetuses with Down's syndrome and thence to termination of pregnancies, the money could be directed to research into fundamental solutions. An analogous calculation can be made at a national level: In the Netherlands it seems likely that some 300 foetuses with Down's syndrome can be detected annually, as estimated from the number of live births corrected for spontaneous abortions. If, in a financial sense, every foetus identified indeed costs the same as two researchers with some provision for overheads, one is talking of an approach which could fund a group of 600 researchers in the Netherlands alone. Particularly when one thinks in global terms it seems highly likely that even a partial redirection of effort in this manner could provide the tools needed to modify and perhaps even prevent the development of Down's syndrome.

2.5. Conclusions

1. In the Netherlands there is an urgent need for accurate, recent data on prenatal diagnosis and follow-up of cases of Down's syndrome.
2. Counselling practice for couples at risk of bearing a baby with Down's syndrome should be changed markedly, with the involvement of syndrome-specific organisations and of other parents.
3. The option of carrying a pregnancy of a baby with Down's syndrome to an end after a positive outcome of prenatal diagnosis should be given at least the same weight as the option of termination.
4. The necessary research should be conducted to solve the problem of Down's syndrome in a fundamental way, without the need for termination, by working towards biochemical intervention as well as identifying means of primary prevention.

Acknowledgement

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References

- [1] E.A.B. de Graaf, Down's syndrome in the Netherlands, *NVDA Nieuws* 22(5) (1995), 26–29 (in Dutch).
- [2] H. Wolf, G.M.C.L. Christiaens and N.J. Leschot, *Annual Review 1990* (Jaarverslag 1990, in Dutch), Werkgroep voor prenatale diagnostiek van de Nederlandse Vereniging voor Obstetrie en Gynaecologie en de Vereniging Klinische Genetica Nederland, 1993.
- [3] M. Cornel, Eurocat Groningen, Personal communication, 1994.

- [4] Anonymous, *At the Cradle of the Future: Scenarios for Care in Relation to Human Reproduction 1995–2010* (Aan de wieg van de toekomst; scenario's voor de zorg rond de menselijke voortplanting 1995–2010), Stichting Toekomstscenario's Gezondheidszorg (STG), 1994 (in Dutch).
- [5] E.A.B. Graaf and M. De Graaf-Posthumus, The future of Down's syndrome, *UpDate* **12** (1995), 5–8 (inside Down + Up, no 32) (in Dutch).
- [6] G.H. Verrips, R.A. Hirasing and M. Fekkes, Evaluation Down Syndrome Team, Report PG 95.057, TNO Prevention and Health, 1995, 193 pp. (in Dutch).
- [7] G.H. Verrips, R.A. Hirasing, M. Fekkes, A.G.C. Vogels, E.A.B. De Graaf and S.P. Verloove-Vanhorick, Health related quality of life in 0–8 year old children with Down syndrome, *Quality of Life Research* (in press).
- [8] J. Busciglio and B.A. Yankner, Apoptosis and increased generation of reactive oxygen species in Down's syndrome neurones *in vitro*, *Nature* **378**(6559) (21–28 Dec. 1995), 776–779.
- [9] J. Lejeune, *Presentation at the 3rd World Congress on Down's Syndrome in Brighton*, England, 1986.
- [10] T.E. Elkins and D. Brown, Ethical concerns and future directions in maternal screening for Down syndrome, *WHI* **5**(1) (1995).

3. Prevention of congenital anomalies: policy in the Netherlands

Prof. E. Borst-Eilers

Minister of Public Health, Welfare and Sports, the Netherlands

3.1. Introduction

The prevention of congenital anomalies is one of those matters which are influenced by the dynamic developments in biomedical research taking place within the domain of human procreation. Our diagnostic possibilities and our understanding of genetic and other determinants in the aetiology of malformations and disease are rapidly increasing. These developments require careful consideration. On the one hand the expanding body of knowledge can offer people choices in situations where previously their fate was preordained; on the other hand it can also cause suffering. In addition it places us before difficult dilemmas.

Hence, there are many questions of ethical, juridical, sociological and psychological importance which need to be addressed and to be balanced against the insistent forces of scientific endeavour. The subject tends to arouse ideological, religious and political sensitivities, which may sometimes inevitably burden our clear reasoning with an emotional factor.

Medical interference with human procreation therefore needs a very careful approach by all those who have to deal with it: physicians, researchers, parents and patients and their advocacy organisations, health educators, the media and last but not least the government. All the parties involved should listen to each other's arguments with an open mind.

In order to know what we are talking about, a clear picture of the epidemiology of congenital anomalies is needed at the outset. I therefore wish to stress *in the first place* the value which the Dutch government attaches to adequate registration. *Secondly*, I will discuss practices and attitudes toward secondary prevention or intervention and the ethical issues involved. *Thirdly*, I would like to say something on primary prevention, especially on the folic acid issue.

Finally, I should like to ponder a little over the socio-cultural setting of prevention and the importance of a well-informed ongoing public debate on the prevention of congenital anomalies.

3.2. Registration

The Netherlands Ministry of Health financially supported the Dutch EUROCAT registries from their beginning in 1981 onwards. The first registry was and is located in Groningen (EUROCAT Northern

Netherlands, in the University Department of Medical Genetics). In 1990 a second registry was established in Rotterdam: EUROCAT SouthWestern; this is situated within a Municipal Public Health Service. The data provided by EUROCAT have been very useful and the Ministry intends to continue its support during the coming years. It is to be hoped that these activities will contribute to the prevention of congenital anomalies in the future.

More recently several other organisations have called for the creation of a national registry of birth defects: they comprise the Vereniging voor Samenwerkende Ouder- en Patientenorganisaties (VSOP, Alliance of Collaborative Parent- and Patient Organisations), The National Institute for Public Health and the Environment (in its report on Public Health Future Explorations) and the Health and the Nutrition Council (in its report on folic acid and neural tube defects). I agree with many of the arguments advanced for such a step, especially since at least 3% and possibly as many as 8% of newborn infants exhibit more or less severe congenital anomalies. The frequency of each individual anomaly is low, and reliable figures are needed – for instance in order to detect as early as possible changes in the incidence of the defect, to identify causes and to set up adequate interventions. Reliable figures are also needed if we are to determine whether health policy measures prove effective. Examples are the national rubella vaccination to prevent congenital rubella syndrome, and the national campaign on folic acid for women planning pregnancy, which was launched in September last year. Good registration and therefore reliable figures may help us to evaluate the effect of such campaigns on the frequency of certain birth defects. However, we have ensured that we avoid over-estimating the incidence of defects, for example, by accidentally recording an individual case more than once.

The present two EUROCAT registries cover 25% of births in the Netherlands. During the recent working conference on “Genes in the Netherlands” priority was given to determining whether national figures on birth defects can be derived through collaboration with ongoing registries. This would be in accordance with our current health information policy; it is obviously important to make optimal use of existing registries, before incurring the expense involved in establishing new ones. I therefore gave financial support to a project that will investigate the possibility of using data from the National Obstetric Registry (LVR) and the National Neonatal Registry (LNR) for the monitoring of birth defects. I also provided extra financial support to EUROCAT Northern Netherlands for further analysis of the data collected since 1981, especially with regard to possibilities for the prevention of birth defects and identification of new risk factors.

In all, the annual financial commitment of the Netherlands government to activities relating to the registration of congenital anomalies amounted to approximately one million guilders in 1996.

3.3. Policies regarding interventions

I now turn to a major theme of this symposium: “Public health and the prevention of congenital anomalies”. When we speak of prevention in this country, we usually refer to primary prevention, though the present programme also extends to presentations on prenatal diagnosis and screening. I hesitate to use the term ‘prevention’ in the context of prenatal diagnosis, as the ensuing possibility of termination of pregnancy – which is always a dramatic step – puts a different face upon this technique. Perhaps we should use the term ‘intervention’. Let me first discuss Dutch policy and, more generally, the Dutch attitude towards intervention and return a little later to the issue of true primary prevention.

Pregnancy is, in the Netherlands, not considered as a health problem, but as a normal physiological situation. Medicalisation of pregnancy and delivery is, in general, regarded as undesirable. The incidence of home deliveries in the Netherlands is 30%, which is higher than in any other Western European

country. We can rely on well-trained and experienced midwives, general practitioners and nurses for the care of mother and child at home. The small distance from home to hospitals also plays a role here: from almost any place in the Netherlands a patient can be transported to a hospital within half an hour. In the event of complications during pregnancy or increased risk, pregnant women are referred to obstetricians.

Ultrasound screening during pregnancy has not become a routine, although 90% of pregnant women at the present day undergo at least one ultrasound investigation. Usually this is performed in the first trimester in order to assess gestational age and exclude a twin pregnancy, or in the third trimester to determine the position of the foetus. Second trimester ultrasound to detect possible congenital anomalies is mainly performed in women who are at an increased risk. The funding of detailed second trimester ultrasound was for a time problematical, but as of 1996 my Ministry made adequate financial arrangements for its performance where necessary.

Nor is *maternal serum screening* to detect neural tube defects or chromosomal anomalies undertaken routinely, though some hospitals, midwives and general practitioners offer this to their patients. Good information is crucial here, since maternal serum screening provides no certainty about the presence or absence of a foetal anomaly, but only an individual risk estimate. We are viewing this technique very critically, because, among other things, the quality of information cannot always be guaranteed.

Prenatal cytogenetic diagnosis has been offered to older mothers in the Netherlands for many years. According to the most recent estimate, it is employed in 55% of pregnancies. Women not using PCD are usually well-informed as to what it can offer, but choose not to have the test done, either for ethical or religious reasons or because a child with Down's syndrome would in any case be welcomed and accepted in their home.

When the Netherlands is compared with other Western European countries, the proportion of cases diagnosed prenatally and the proportion of pregnancies terminated because of congenital anomalies is not very high. Complete prenatal detection of congenital anomalies is not an aim of pregnancy care, nor of genetic counselling in our country. Adequate information to parents is however considered important, and individual choices are respected. Since 1979 the application of advanced prenatal diagnostic techniques has been allowed and carefully planned in seven academic locations in the Netherlands, the so-called *genetic counselling and examination centres*. Expertise on genetic and congenital disorders is here guaranteed, since the same centres are performing genetic counselling, karyotyping and post-natal DNA investigation. Both women and men at risk can be referred by their general practitioners to these centres on individual indication, and these facilities are hence within the reach of anyone who is at increased risk.

The ethics of prenatal diagnostic techniques have been debated regularly since the early 1980's, generally and in professional circles, as well as within the Health Council. This ongoing discussion has helped to clarify the borderline between what are to be considered severe and less severe anomalies and to define the term "health problem". I welcome this debate, because it has made clear that prenatal diagnosis has never been employed lightly in this country. It is not a self-evident routine for women who could be considered proper candidates for it. I also find ample evidence that in those cases where pregnancy is terminated following the outcome of prenatal diagnosis the strictest criteria for careful decision making are met.

Here I should also say something about population screening. In order to regulate the fast-going developments with regard to screening, the Dutch parliament passed a law on Population Screening, which was due to enter into force in the summer of 1996. The Netherlands has now become the first country to pass a law on population screening, a measure that may also have implications for the prevention of

congenital anomalies. The aim of the Act is to protect the population from undesirable screening programmes. This is achieved by subjecting sensitive health-screening programmes to a licence, to be issued by the Minister of Health, acting upon the advice of the Health Council. The Act allows for assessment of the desirability of a screening programme on several criteria; the main criterion is its estimated benefit as balanced against the risks to the health of those who are participating in the programme.

3.4. Prevention of congenital anomalies

In the Netherlands, the primary prevention of congenital anomalies had by 1996 been the subject of two reports to the government, dealing with folic acid and hypervitaminosis A, respectively. I will limit myself here to the folic acid issue.

The Health Council and the Nutrition Council recommended in November 1993 that all women planning a pregnancy should be assured of an adequate intake of folic acid. This provided the basis for a practical recommendation by my predecessor and the Health Inspectorate that 0.4 or 0.5 mg folic acid tablets should be given daily, starting at least four weeks before conception, and continuing until two months thereafter. It is estimated that 90% of pregnancies in the Netherlands are planned; it should therefore be possible to achieve a high proportion of periconceptional use of folic acid tablets. The original level of use had nevertheless left a lot to be desired; early in 1994 it was estimated that folic acid had been used periconceptionally only in 1% of pregnancies. A special information campaign directed to general practitioners, midwives, obstetricians and "well baby" clinics was therefore carried through in the spring of 1995; a further campaign directed to the general public followed in September 1995, comprising brochures, printed and radio commercials and free publicity in TV and health magazines. The campaign was due to be evaluated, with the results determining what follow-up might need to be developed.

In the meantime, fortification of foods with folic acid was announced in the United States on 29 February 1996. This possibility had been considered in the Netherlands after the advice of the Health and the Nutrition Council was published in 1993, but it was concluded that such fortification would arouse much discussion of the type experienced in the 1970's when fluoridation of drinking water was considered. Because of that debate, Dutch drinking water still does not contain fluoride, even though for reasons of Public Health (namely for the prevention of caries) it would be wise; the High Court decided that the consumer's freedom of choice was more important. Since then toothpaste has been fluoridated and parents are advised to give young children fluoride tablets. On the other hand, fortification of salt with iodine and of margarine with vitamin A and D has been accepted for many years. While it was concluded that compulsory fortification of food with folic acid would demand a long discussion, restoration of foods, to compensate for folic acid losses during processing of food products, was approved by the Dutch Cabinet in September 1995. Before going further and pursuing a US-type policy of compulsory fortification of certain foods with folic acid, I would prefer to wait for the results of the evaluation of the awareness campaign, which will hopefully show a substantial increase in the periconceptional use of folic acid tablets.

Finally, I am aware of the potential protective effects of folic acid as regards cardiovascular diseases in adults, spontaneous abortion and some birth defects other than neural tube defects. Hence, I consider it the responsibility of my ministry to take care of adequate folic acid intake in the population, and I shall follow developments closely.

3.5. *Socio-cultural influences and prevention*

Progress in clinical and epidemiological research has greatly improved our understanding of the aetiology of congenital anomalies. Beside the dangers of hypervitaminosis A and of relative folic acid depletion, we now have a far better insight than before into the negative effects of active and passive smoking, alcohol, pharmaceutical and recreational drugs and environmental influences. This whole body of biomedical knowledge might however prove to have relatively little impact on the prevention of congenital anomalies, if what one might call a fertile socio-cultural soil were lacking. The socio-cultural circumstances in the Netherlands are such that most pregnancies are planned and that the decision to have children is the outcome of a positive choice by emancipated adults. As a result of a relative lack of poverty and a good general educational level – including sex education – teenage pregnancies are rare. We have in addition a well-developed system of primary health care, including general practitioners and a low-threshold network of community child health care and prenatal care, which can translate the newest scientific insights into programmatic prevention activities. There are also ongoing health education and information campaigns for the prevention of alcohol and drugs abuse, sexually transmitted diseases and smoking, and for the promotion of healthy nutrition.

These are all ideal circumstances for developing primary prevention of congenital anomalies, starting in the preconceptional phase. There is however still a great deal of work to be done in order to raise public and professional awareness in this specific area. I am convinced that some progress can be attained by making better use of the existing possibilities for counselling and early diagnosis. At this moment, therefore, I see no urgent need for setting up extra facilities for pre- and periconceptional consultation. I do however fully support the activities of the VSOP (Alliance of Collaborating Parent- and Patient Organisations), a body which is invaluable both for the lay public and for professionals. The VSOP does not only function as a source of information; it also makes a sustained effort to reflect on the ethical, legal and social aspects of congenital anomalies, following activities in this field for more than 20 years. The VSOP was indeed one of the initiators of the “World Alliance of Organisations for the Prevention of Birth Defects”; it actively supports the contribution of parents and patients in the public debate on issues relating to prevention of congenital anomalies, screening and prenatal diagnosis. Such a debate took place, for instance, in February 1995, under the auspices of the National Platform for Science and Ethics, instigated by the Netherlands Parliament. The VSOP plays an important role in ensuring meticulous policy development in an atmosphere of openness and with respect for divergent individual opinions. This too is, I believe, a socio-cultural factor, which positively influences the prevention of congenital anomalies in the Netherlands. The government should not monopolise the discussion, but give room to the other parties involved.

My policy supports development towards increasing assumption of responsibility by patients, who want to decide on all issues relating to the quality of their lives and the lives of their children. The role of the government is and must be to promote an adequate supply of information and a free interchange of moral opinions so that individuals can decide in complete freedom. We must provide assurances that at any time there will be a place in our society for handicapped people. Primary prevention of congenital anomalies on the one hand and care for handicapped children and adults on the other are therefore both important goals of our health policy. Above all, I would express the hope that against the background of this national policy, parents and doctors will be enabled to take the right decisions in the face of the rapid developments offered by medical progress.

4. Preventing congenital abnormalities: highlights of the discussion

Is prenatal screening or diagnosis, followed by termination of pregnancy, to be considered as a form of “prevention” of congenital defects or is it better to use the term “avoidance” or “intervention”?

N.J. Wald: It’s really a question of language, and I think if people understand what is meant, it is probably not helpful to dwell too long on it. Having said that, I do feel so uncomfortable about using the word prevention in the context of antenatal screening, diagnosis and selective abortion. I would prefer to restrict the use of the word prevention to efforts to identify people who may get the disease and to genuinely reduce its frequency such as we can by the use of folic acid in neural tube defects. Semantics apart, being able to offer screening to entire populations does offer the possibility of avoiding the majority of serious handicaps and congenital disorders with the means already available. A central issue is whether health agencies should offer this service systematically in a compassionate and well-informed way, with support provided, or whether one should simply institute the service and wait for people to ask for it. If it is necessary to apply for testing it cannot be considered a true screening situation, since those people who do apply are thereby expressing a specific concern.

Can the money which is spent on prenatal diagnosis be better used to carry out more research on primary or secondary prevention, as suggested in the paper by de Graaf and de Graaf-Posthumus?

E. Borst-Eilers: Answering questions about money is the task of the politician, but let me first react briefly to what Dr Wald has said. Formally and personally, I have no objection to using the term prevention when we talk about prenatal diagnosis, because I agree with Dr Wald that if you know what you mean by it, and that is understood, than it’s a semantic question. As a minister, however, I of course have contact with several organisations of people who are handicapped themselves, or who have handicapped children; they are very sensitive about this, feeling that using the word prevention for this is too easy and is covering something up; in effect, they say, you “prevent” the disorder by killing the foetuses who carry it; this they find painful, and that I entirely understand. On the other hand, I am, as I said in my paper, all in favour of making what most people regard as the advantages offered by medical progress available to the population. Many men and women dare start a pregnancy, despite having a very serious defect in their family, so serious that they didn’t want one of their children to have to live with that defect, because they know there is the possibility of prenatal diagnosis and termination of pregnancy. And they think it’s a wonderful thing that this is available. In addition, if I look at what our parliament has been saying on this issue, one can now regard these services as an accepted part of medical care in this country. I therefore see no reason whatsoever to stop spending money on prenatal diagnosis.

What is the background to the divergent policies of countries regarding the periconceptional use of folic acid?

D. Erickson: Such recommendations depend to some extent upon the perception within the health authorities concerned of the fraction of pregnancies, which are planned, and the fraction which are unplanned. In my own country (the USA), where 50% of pregnancies are unplanned and unanticipated, we felt in the public health service that it was nevertheless very important to try to get folic acid to all women; this necessarily drove us towards the idea of food fortification. The situation in the Netherlands, where most pregnancies are planned, and folic acid can be part of the planning, is obviously different. That also seems to apply in the Peoples Republic of China, where pregnancies seem to be not merely planned but actually licensed.

If I might make a comment about fluoridation: in many countries including the United States, the “anti-fluoridationists” have been very powerful in lobbying against the fluoridation of public water supplies. Despite that, about 60% of public water supplies in the United States are fortified with fluoride at the level of 1 mg per litre and caries rates have since dramatically decreased. I think it has been a great public health success, but clearly the anti-fluoridationists have kept it from being universal in the United States. Naturally, we are not speaking of a mere hysterical reaction: fluoride is a toxic substance – 1000 mg and you drop dead, and 20 mg a day can induce crippling fluorosis in the long term. By contrast, folic acid is by contrast non-toxic. The only concern here is that it may relieve the anaemia which accompanies vitamin B12 deficiency and thereby mask the latter.

N.J. Wald: The answer to the above question lies in political and social philosophy and culture, not in science. I recognise the argument that folic acid might mask vitamin B12 deficiency, but most medical authorities now say that the latter can be diagnosed even in the absence of anaemia. When the possibility of folic acid fortification of food was discussed in Britain, one senior person said: “Oh no, it’s going to be fluoride all over again”. I could only remark: “Yes, but fluoride was good.” Some good policy measures take courage, political courage, and this is one of them. For those who object to fortification there is a way out: nobody is arguing that one will be prohibited from buying or selling non-fortified bread or flour, even in America. What has been proposed is simply that fortification will be the norm, as it is in Britain where bread is already fortified with thiamine, niacin, calcium and iron. Those individuals who want to buy the non-fortified product can still get it, but they will have to make the effort. Actually, in Britain I see no public opposition to the fortification of flour. Almost every agency in Britain has been consulted; the Spina Bifida Association and the consumer groups have all supported it and they have all asked the government: “Why aren’t you doing it?”

E. Borst-Eilers: I have come to the conclusion on this folic acid issue that here in the Netherlands, the best way to go about it is first to try and achieve our aim by what I just described; an information awareness campaign, the success of which will have to be evaluated. Most probably it will have some effect, but not prove totally successful. If that is the finding, I shall be able to go to parliament with a firmer argument to win them over to the idea of fortifying food. Had we proposed folic acid fortification without such evidence I would have anticipated unsurmountable opposition; and if you lose the debate once, it is all the more difficult to win it later.

There is a difference between screening and diagnosis. Screening involves selecting a part of a population at sufficient risk to justify undergoing a diagnostic procedure. Some people consider serum screening insufficiently reliable, since there are more false positives and false negatives than in a diagnostic test, but age screening is even less reliable. If there is now a Dutch law on population screening, should it take into account ultrasound screening for chromosomal anomalies as well?

E. Borst-Eilers: Yes, I believe that all existing and future programmes offering a diagnostic procedure to people who are not aware that they are at that moment at a higher risk or have a disease, fall within the terms of that new Act. First, the Health Council will have to look at the question “is this one of those programmes which the law has in mind when it says that you need permission from the minister?” Some of these screening programmes will merely be registered, and no licence will be necessary. A few defined types of programme will need a license.

L.P. ten Kate: Does that mean that maybe the Health Council will say: “Prenatal diagnosis for advanced maternal age does not fulfil the criteria, so we should stop it?”

E. Borst-Eilers: No, the Health Council can never say stop or go. It can either say that a programme has to be put before the minister or need not be put before the minister, and then they advise the minister,

it's always the minister; who decides, it remains a political decision. And of course parliament wants to share in this decision. The Health Council will essentially have to tell myself and my successors the scientific facts relating to a particular type of screening – what type of screening is it, what are its clinical benefits and what are the potential health risks. The political decision will be based on that information.

Serum screening is viewed critically in the Netherlands, both by politicians and by the majority of parliament. It is well understood that such screening provides no more than a risk estimate, and that it does no physical harm. The parliamentary majority however fears that since women here in the Netherlands are accustomed to diagnostic procedures which give a clear answer they will expect a black-and-white answer in this case as well. The concern would be less if there were certainty that women – most of whom are not familiar with risk estimates – could be given the result accompanied by a full explanation as to what it does and does not mean. The current situation is that both the scientific and psychosocial aspects of serum screening are being looked at; a project could well be designed and budgeted in due course by the Health Fund Council. After that the definitive decision will still have to be taken as to whether we shall introduce it in this country, making it analogous to the diagnostic testing which we routinely perform on women above 36 years of age. Hesitation to date has come not from the scientific world but from those concerned with the sociology, the ethics and the politics of such screening. If this can be resolved, the way to such screening will I think be open.

N.J. Wald: I must admit to some concern here. In our own hospital, we already have a clear result. By age- and serum-screening 100,000 women, nearly 5000 amniocenteses were avoided that would have been indicated if we had used age screening alone; assuming that amniocentesis results in 1% foetal loss, we thereby essentially avoiding losing 50 normal babies. What is more, by using serum screening, 60 more cases of Down's were detected. This approach is therefore justified. And if something is more effective and safer than what has gone before, surely it's the duty of Ministries of Health to promote that technology, provided it's affordable.

E. Borst-Eilers: I think you should have had a participant in this forum who was personally critical of this technique, so as to balance and enliven the debate. I am speaking here as a minister and in such a sensitive area as this a minister can be restrained by a hesitant parliament. This is a muddled situation, but we have to take all views into account.

S. Aymé: In France, too, we experienced a heated debate as regards serum screening in pregnancy. France was the first country with a national ethics committee, and also the first with a law on bioethics, which dates from July 1994. In 1990 we decided to undertake a pilot policy study, exactly what you are describing for the Netherlands. The aim was to reach conclusions on how feasible it was, what the adverse effects of such a programme might be and so on. A programme was carried through on 20,000 pregnancies during a year and the report was published. It showed clearly what Nicholas Wald is saying, i.e., that it's much more effective than merely screening on the basis of age. However, we also found that it was not so easy to implement such a programme, that the laboratories had to be very reliable, and they had to be very well organised with their colleagues in cytogenetics and genetic counselling and so on. The whole story ended in a decision that such a programme should be only instituted if it is well organised. This meant we needed to have clear guidelines on how to carry out the screening procedure. Before any decision was taken, the Minister of Health decided to seek the advice of our National Ethics Committee, which was published in 1993. Surprisingly enough, the advice given was that to screen through markers was more ethical than screening through age, since all the women could get the test, which was more in agreement with the principles of equity and fairness. The Committee therefore recommended continuing with serum screening. The law of 1994, which was passed, listed serum screening for Down's syndrome as one of the tests which could culminate in prenatal diagnosis,

and for this reason it was ordained that testing could only be performed in accredited labs. As of 1996, laboratories have been seeking accreditation. The result is that only half of them have been found to merit accreditation. We hope that by involving only these centres the programme will be able to continue smoothly, and rather better than in the past, when the testing was widely demanded both by physicians and pregnant women, but was not always well performed. In conclusion: there is no rationale against this test and it indeed has ethical merit, but it must be organised properly.