Screening for phenylketonuria in a totalitarian state

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Abstract

Living under a totalitarian regime has many effects on the structure, way of thinking, and relations in a society. However, it is the impact on neonatal genetic screening that we discuss in this paper. Genetic screening functions at the interface between health services and society at large. Being involved for over a decade in setting up the Bulgarian PKU screening programme, we have had to deal with ways and attitudes which may be difficult for the western mind to grasp. Yet comprehension is very much needed in the new world we are trying to create.

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In the early seventies, mass screening of newborn infants for the early detection and treatment of PKU became a routine component of preventive medicine in most European countries. The Bulgarian screening programme was started in 1978 as the result of pressure exercised by a small group of experts and the Ministry's ambition for initiating 'prestigious' programmes in maternal and child health care.

A decree of the Ministry of Health declared blood sampling of newborns mandatory and postulated that screening tests would be performed by a central screening laboratory and treatment of patients would be the responsibility of the Sofia Institute of Paediatrics. Preparation for the screening was thus considered completed.

The laboratory component¹

The staff at present involved in the screening programme includes one medical doctor, two laboratory technicians, and a part time medical secretary. The laboratory is situated in the Institute of Obstetrics in an area of 15 m². It is involved in screening all the newborns in the whole country (about 120 000 annual births) and also in the follow up and diagnostic analysis of screening infants with a positive test and in the biochemical monitoring of the dietary treatment of PKU patients.

The Guthrie bacterial inhibition assay is used for screening the dried blood samples and quantitative fluorimetric phenylalanine determination is performed immediately on samples with positive or borderline results. This two stage screening procedure, together with the procedure used for haemoglobin inactivation (formic acid vapour instead of autoclaving) have helped to keep the recall rate below 0.1%. Quality control was part of the programme from the outset and included an intralabora-

tory precision component and an interlaboratory accuracy component (the Japanese quality control system).

In 12 years, the laboratory has tested nearly one million newborns. Two PKU cases have been missed (one bipterin deficiency with phenylalanine values on day 3 falling within the normal range and one classical PKU where the poor quality of the blood sample resulted in a spuriously normal phenylalanine value).

The laboratory component of the Bulgarian neonatal screening programme is very similar to its equivalents elsewhere and is probably of limited interest to the international community of geneticists. The dissimilarities appear where the analytical aspects end and where the interface between a genetic prevention programme and society at large begins. Living in a totalitarian state has many effects on the structure and way of thinking of a society and it is the impact on genetic screening that we would like to discuss.

Genetic screening and centrally planned economy

In the planned economy of Bulgaria, health care was funded from the central state budget on a 'residual' basis. In practice, this meant that public health was, as a rule, underfunded and under constant pressure to satisfy the overwhelming immediate needs of hospitals and sick patients, etc. The needs of a handful of mentally retarded patients were therefore a very low priority.

Central funding had an impact which one might call the 'anonymity effect'. With the state assuming for decades the role of the care provider, the source of funding gradually became anonymous in the minds of the public. Therefore, the very concept of decision making based on cost/benefit analysis was alien to the health administration. Since it was not clear who paid for the care of the mentally retarded, it was also nobody's concern to invest in the prevention of mental retardation. Prevention programmes did exist but they were motivated by reasons such as prestige and imitation and had nothing to do with the economy. In this context analysing the efficiency of the programmes was not only unnecessary, it was inconceivable, as it might result in 'unprestigious' conclusions.

Equity and free access, which were the basic concept of health care, gradually degenerated in the minds of the consumers and also of decision makers to the notion that health care is in fact free of costs. In practice, this resulted in the sheer inability of public health administrators to think in economic terms and plan the

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funding of all and every component of a prevention programme.

All three factors had a profound effect on the neonatal screening programme. In the decision of the Ministry of Health to start the programme, funding was not mentioned. As it turned out, the problem had not even been considered. In a centralised economy the major component of a screening programme, namely overhead expenses, is covered by an anonymous source and therefore is of no concern. Labour was cheap anyway, therefore this component was negligible. The problem of analytical expenses was implicitly delegated to the screening laboratory and was solved by its dedicated staff by (1) reducing the costs to a minimum of \$0.05 per sample and (2) ingeniously charging the costs to sources inside the Medical Academy (a huge teaching and research hospital) and alternating the sources each year.

The need for funding came as an unpleasant surprise when the programme faced the problem of treating the PKU patients it had detected. An ultimate decision was never reached and the problem was raised and somehow solved on an ad hoc annual basis. As a result the overall quality of dietary control was poor and a large proportion of the blood samples of patients under treatment showed raised phenylalanine values, thus reducing the benefit of the screening programme.

Unlike the laboratory component, which was organised and ready to function rapidly, the uptake of the screening programme by the health services took a decade and even today is less than complete. The highest coverage of newborns was reached in 1988 and was about 90%. A substantial proportion of PKU cases (over 15%) were missed by the screening because a blood sample was never taken and have developed various degrees of mental retardation.

Thus the anonymous care-provider took the triple load of running the screening programme, purchasing the dietary foods, and in the long run taking care of the mentally retarded patients produced by inadequate treatment and incomplete coverage. The problem of efficiency was repeatedly raised by the screening laboratory but a discussion has never been possible because of lack of response.

Genetic screening and the medical profession

The unwillingness of health professionals to cooperate in the neonatal screening programme was the end result of several synergistic effects. PKU screening was no special case and the same attitude has had a serious impact on the overall uptake of genetic services in the country.

Teaching genetics had been a taboo for years and had been reinstituted shortly before the screening was initiated. The programme therefore had to rely on the participation of physicians who knew only intuitively that heredity exists but had no idea about its mechanisms and mistrusted the very idea of

genetic prevention. A more general problem of medical education in this country lies in the inability to present medicine as a constantly growing field and create an open framework into which new developments can be incorporated. This results in a health care system which is inert or even hostile to the transfer of advances in research to every day patient care.

In addition, a general dissatisfaction with underfunding and the inadequacy of health care facilities and technology, together with the low priority given to mental retardation in the overall structure of child health care, made the screening programme look like a bizarre undertaking of the central authorities.

These problems could have been foreseen had serious consideration been given to the efficient organisation of the programme. However, the national health system as it operated in Bulgaria was very hierarchical and the participation of primary care physicians in any programme was considered to be a matter of obligation which required no previous discussion. There was nothing to fill the gap between unrealistic ministerial attitudes and an indifferent and refractory health care system. With lack of analysis, even the existence of the gap was not realised.

Genetic screening and the issue of human rights

In a system where the state assumes the role of a caring mother whom citizens are expected to trust, the concepts of individual responsibility and informed consent are non-existent or have a distorted meaning. Since any decision taken by state authorities is to the benefit of the individual citizen, acceptance and obedience are the only responses to be anticipated. This is true with regard both to those who have to implement the decision and to those for whose benefit it has been taken. On a smaller scale this kind of relationship has also become the rule between health professionals and patients.

The impact on genetic screening had different aspects. The informed consent of parents has never been regarded as a mandatory component of a successful screening programme and the laboratory has seen many families where a positive screening result came as an unexpected shock. The lack of public awareness and support also resulted in some parents refusing their permission for a repeat test, in excessive undue concern caused by borderline phenylalanine values or in lack of compliance with dietary treatment. This was often aggravated by the unwillingness or inability of local physicians to provide a reasonable explanation to the families, both because physicians themselves were not sufficiently well informed and because engaging in a dialogue is not part of the traditional authoritative role of the doctor.

Lack of personal responsibility of health professionals in cases when a PKU patient has been missed by the screening is complemented by the submissive role of the family in the relationship. This is a component of the overall social hierarchy and bringing a missed

PKU case to court seems unthinkable to all parties involved.

The issue of human rights in Bulgaria acquired a special meaning in relation to the ethnic conflict in the eighties. Forcing the Islamic population of Bulgaria to adopt Christian names first started with the gypsies and subsequently included the ethnic Turks. This affected the newborn screening programme in two ways. Galactosaemia was initially part of the screening programme and a very high frequency of galactokinase deficiency was detected among Bulgarian gypsies. The publishing of these data was impossible because it implied admitting the existence of this minority group to the international community. Much more serious harm, however, was suffered by the programme registry. Changing the names of ethnic Turks was accompanied by an irresponsible and again anonymous decision to destroy all medical records and thus leave no trace to suggest that Moslem names ever existed. This criminal decision was all the more absurd as it took no account of the fact that such names could be found in readily available sources, such as telephone directories. The national PKU screening laboratory was one of the few which secretly disobeyed and kept the records. However, with the change of names it became very difficult and confusing to maintain a registry, especially when a retrospective search of a screening sample was required.

In the summer of 1989 an exodus of ethnic Turks from Bulgaria took place. Among them were many PKU families whose immigrant status and inability to pay for the dietary foods in the new country of residence has probably resulted in the mental deterioration of the patients. Although far from perfect, dietary treatment of PKU in Bulgaria was somehow ensured. The migration of a significant proportion of the ethnic Turks has had an additional effect on the screening for PKU. With a higher incidence of the disease among Turkish children, it will result in a lower efficiency of the programme with fewer PKU cases detected.

Neonatal screening in Bulgaria today

The fact that the programme continued to exist and gradually gained strength was a mira-

cle of professional dedication. In order to educate medical professionals and motivate the primary health care system to participate in the screening, the laboratory has engaged in direct contact with all 124 maternity hospitals in the country. Each year new Guthrie cards are distributed by the laboratory to the maternity wards and are accompanied by an annual report on the progress of the programme (for the whole country as well as in the specific region and hospital). Descriptions of missed PKU cases are also posted to all participating in the programme and contain an analysis of the reasons and consequences. Requests for a repeat blood sample are accompanied by detailed explanations and suggestions on how to approach the parents.

The screening laboratory, which is now part of a larger biochemical and molecular genetics unit, has become widely known to primary health care personnel and the programme is gradually becoming routine. A PKU society has been founded and parents are gradually learning to exert pressure and ask for better treatment. The main merit of the PKU screening programme is that it stimulated interest and awareness and managed to create a functioning structure.

Neonatal screening in Bulgaria tomorrow

General discontent and the strong desire for change place the emphasis on privatisation as a panacea to all problems of health care in Bulgaria. With lack of awareness and tradition in genetic prevention, persisting poor quality of education in human genetics, and no respect for the rights of couples at risk to make informed reproductive decisions, privatisation and the collapse of the national health system will postpone indefinitely the implementation of genetic services in primary health care.

At present, the situation is complicated further by the illusion that western aid in terms of high technology will help to circumvent problems whose nature requires a different kind of effort. It is better understanding on both sides, rather than high technology, that will give this country a better chance.

1 Kremensky I, Kalaydjieva L. Avoiding sources of error in PKU screening. *Am J Clin Pathol* 1989;92:396-7.