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redactie:
h. j. m. messerschmidt, biochemicus, rosmalen
j. a. p. van parijs, arts, heemstede
dr. g. a. roelofs, zenuwarts, assen
e. h. j. smeets, biochemicus, maastricht
j. h. h. verbeek, internist, rosmalen
redactieadres:
h. schrevel, ziekenhuiscentrum, oudlaan 4, utrecht, tel. 030-739911
administratieadres:
de tijdstroom, bagijnestraat 11, lochem, tel. 05730-1264

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Special issue on the occasion of the third international congress of the international association for the scientific study of mental deficiency

The Dutch institutions for the mentally retarded and the psychiatric hospitals have in the post-war years passed through an important evolution.
The renewed inspiration of the activating therapy as well as the introduction of psychopharmaca caused an unknown development on nearly every field of practical acting.
Therapeutical results increased sharply, though important problems still lay ahead.

A major development of the last few years linked together the different institutions, as well on the administrative as the executive level. Since 1968 one national association, the Nationale Ziekenhuisraad, holds nearly all health care institutions. The section psychiatric institutions of this association has a membership consisting of 86 institutions for the mentally retarded and 76 psychiatric hospitals.

The increasing sense of solidarity and of a shared responsibility for institutional health care in our country resulted in 1967 into the institution of the Coördinatiecommissie Biochemisch Onderzoek, a committee for the co-ordination of biochemical research. The committee was set up by the Vereniging van Psychiatrische Inrichtingen in Nederland and the Katholieke Vereniging van Inrichtingen voor behandeling en verpleging van geestelijk gestoorden, the two religiously based associations, which since 1968 form the section psychiatric hospitals of the Nationale Ziekenhuisraad.
Objectives of the committee are:

a. initiating, stimulating, co-ordinating and financing, long term biochemical research;
b. giving advise about the operation of biochemical laboratories in psychiatric institutions;
c. regularly organising scientific meetings on biochemical research;
d. publishing and circulating an informative bulletin;
e. registering biochemical informations obtained from psychiatric institutions;
f. organising and financing certain biochemical

Epidemiological aspects of mental retardation in relation to the genetic mucopolysaccharidoses in the Netherlands***

M. A. H. Giesberts *, A. A. Kroes * and J. J. van Gemund **

Summary

A description of techniques used for the investigation of urinary glycosaminoglycans (GAG) leading to the diagnostic classification of GAG-storage diseases is given.
Out of 700 cases, over 80 patients with Hurler's, Hunter's or Sanfilippo's disease, all three types giving rise to mental retardation, were detected and classified.
Sanfilippo's disease is the most prominent disease among the GAG-storage diseases in Holland and equals the frequency of phenylketonuria among patients with mental retardation in institutes.
It should be kept in mind that Sanfilippo patients do occur in the group of patients with a slowly progressive dementia of otherwise unknown origin.
In addition to the more frequent röntgenologic finding of a thickening of the calvarium, diarrhea was a relatively common finding in this special group.
The possibility of antenatal diagnosis by means of analysis of amniotic fluid-GAG is briefly discussed.

Introduction

Mucopolysaccharidoses or glycosaminoglycans (GAG) storage diseases may give rise to very severe symptoms, depending on the type of disease. Among these are growth disturbances, mental retardation, skeletal malformations, corneal clouding, deafness, joint stiffness, hepatosplenomegaly, epilepsy, and a typical gargoyle-like facial dysmorphism. Based on clinical symptoms and biochemical, radiological, and genetic data, Mc Kusick (1) proposed a classification of the GAG-storage diseases into six types. This classification was extended in 1970 by Horton (2) with another type.
As is now known, the GAG-storage diseases, being inborn errors of metabolism, belong to the group of lysosomal disorders (3,4) in which the deficiency in a lysosomal enzyme (acid hydrolase) prevents the normal catabolism of macromolecular structures; e.g. GAG in the lysosomes. As a consequence, intra-lysosomal storage of indigestible material takes place.
The symptoms mentioned are not yet fully understood on the basis of the storage phenomenon.

As in all other inborn errors of metabolism, early (even antenatal) detection of patients and genetic counselling of the parents are of great importance.
In recent years, the enzyme deficiency in a number of GAG-storage diseases has been discovered (5, 6, 7, 8, 9). In the near future, this may lead to the possibility of detecting the enzyme deficiencies by means of investigation of leucocytes, cultured skin-fibroblasts, or even serum.
Infusions of normal plasma and normal (compatible) leucocytes to patients have been attempted as a therapeutic approach (10, 11, 12, 13, 14). These trials, however, proved to be not very rewarding. Perhaps the liposome approach (15, 16) might be a more promising 'therapy'.
Epidemiological data on genetic GAG-storage diseases are very scant. This may be due to the fact that up to now health authorities are rather unfamiliar with these types of patients. Data are needed, for instance, on the relative frequencies of the genetic types, as e.g. the Sanfilippo-type nearly always will demand permanent residential care. In this respect, we want to report on the results of an investigation in which ± 700 suspect cases were studied. These cases were obtained from pediatric hospital, and mental institute popu-

* Dept. of Pediatrics, University Hospital, Leyden.
** ~~Dutch~~ Institute for Preventive Medicine TNO Leyden.
*** Communication from the Interdepartmental Group for the Study of Lysosomal Storage Diseases, Medical Faculty, Leyden.

Netherlands

lations throughout the country in the period 1970-1972.

We did not perform a classical population survey. This would be an unjustifiable waste of time and money given the low incidence of these diseases. Over 80 cases proved to have an increased GAG-uria. Analysis of urinary GAG in these cases enabled us to classify these patients. As far as mental retardation is concerned, only 3 types are of importance. These are Hurler, Hunter, and Sanfilippo. They will be discussed here at length. For an excellent review covering the whole field of the systemic mucopolysaccharidoses, see Spranger (17).

The classification of genetic GAG-storage diseases with and without increased GAG-uria

The classification of Mc Kusick (1) extended by Horton (2) includes 7 types of GAG-storage diseases all with increased GAG-uria. Table I lists these types.

Another type is described by Suschke and Kunze (18), but the conclusions of these authors might be premature.

More consideration should be given to the descriptions given by Thomson (19, 20) and by Philippart and Sugerman (21) of patients with increased urinary excretion of chondroitin-4-sulphate.

Discussion of the classification of related diseases such as fucosidosis, mannosidosis, I-cell disease, and the mucolipidoses (for a review see Spranger and Wiedemann (22)), in which GAG-storage is not associated with increased GAG-uria, falls beyond the scope of this communication. Though other classifications have been suggested (4, 23), a definite classification based on the specific

Table I

The GAG-storage diseases according to McKusick (1) and Horton (2).

Type	Clinical Picture	Heredity	GAG-uria
I Hurler	Severe mental retardation Early corneal clouding Dwarfism Gargoyle-like facies Hepatomegaly Skeletal deformities	Autosomal recessive	Hep-S * Derm-S
II Hunter	Milder symptoms Moderate to severe mental retardation Absent to negligible corneal clouding Hepatomegaly Early deafness Skeletal deformities	Sex-linked recessive	Hep-S Derm-S
III Sanfilippo	Severe mental retardation No corneal clouding Hepatomegaly Deafness Mild skeletal deformities	Autosomal recessive	Hep-S
IV Morquio-Brailsford	Specific spondylo-epiphyseal dysplasia Normal intelligence Late corneal clouding	Autosomal recessive	Ker-S
V Scheie (-Ullrich)	Normal intelligence Marked corneal clouding Mild skeletal changes	Autosomal recessive	Hep-S Derm-S ('Spät Hurler')
VI Maroteaux-Lamy	Normal intelligence Severe bone abnormalities Corneal clouding Dwarfism Hepatomegaly	Autosomal recessive	Derm-S
VII Horton	Normal intelligence Normal growth Corneal clouding only detectable with slit lamp	Autosomal recessive	Hep-S Derm-S

* Hep-S = heparan sulphate, Derm-S = dermatan sulphate, Ker-S = keratan sulphate.

enzyme deficiencies is not yet available, and the Mc Kusick classification is the most widely used up to now for descriptive purposes.

The variability in the expression of the clinical symptoms within a given type and the overlap of the symptoms between the types are very serious difficulties in assessing the correct diagnosis solely on clinical and genetic grounds.
Biochemical analysis of the urinary GAG is of great help in this respect because, as can be seen from table I, the GAG excretion pattern is related to the type of disease. As will be shown later, it is even possible, by further biochemical analysis, to assess the correct diagnosis on biochemical data only (24).
There is no doubt that investigation of urinary GAG is still the fastest way to confirm the diagnosis 'GAG-uria' and to make a classification of the patient. As far as mental retardation is concerned, three types give rise to severe mental retardation and as a rule to early death. These types are Hurler, Hunter, and Sanfilippo and they will be dealt with further.
No distinction will be made between the known subtypes of Hunter and Sanfilippo (25, 5, 6, 7).

Indications for investigation for GAG-storage diseases

Every child with mental retardation of unknown origin, a gargoyle-like facies, an enlarged liver, skeletal dysplasia and/or dwarfism, especially in association with corneal clouding or another of the symptoms listed in table I, should be investigated for GAG-uria and GAG-storage diseases.
Due to skeletal deformities the liver is not always palpable.

Screening procedures

Many screening procedures are suggested in the literature. For a recent review, see Pennock (26). These tests are based on two principles. The first group of tests uses the metachromasia of the GAG with toluidine blue as an indication for the presence of increased urinary GAG. The second group of tests is based on the turbidity obtained by mixing the GAG-anions with other, cationic, (macro)-molecules such as albumin, CPC (cetyl-pyridinium chloride) or CTAB (cetyl-trimethyl-ammonium bromide). As can be easily understood, the turbidity tests are strongly dependent on pH and total solute concentration.
In our hands, the metachromatic staining with toluidine blue proved to be insensitive and the other tests also gave disappointing results.
From the structure of the GAG (see, for instance, Brimacombe and Webber (27)), it can be derived that in all urinary GAG, except keratan-sulphate (Ker-S), uronic acids (mainly glucuronic acid and iduronic acid) are important components. Uronic acids in GAG can be easily determined by means of the carbazole reaction.
Therefore, we used the uronic acid determination in urinary GAG as a screening for GAG-uria.

Carbazole reaction

As bacterial hyaluronidases break down urinary GAG at a high rate, collection of urine should be done on ice. A 24 h urine specimen is necessary in order to calculate the 24 h uronic acid output. Prior to analysis, these specimina should be kept at —15°C. No preservatives should be added, as these may interfere with the subsequent procedures.
Urinary GAG can be isolated, though not quantitatively from urine by CTAB- precipitation under controlled conditions, according to Di Ferrante and Rich (28).
Purification of the crude GAG preparation is carried out by repeated washings with Na-chloride saturated alcohol (28). After dissolving the GAG in diluted NaOH (0,05 N), the uronic acid is determined by the carbazole reaction according to Dische with the modification of Bitter and Muir (29, 30).
We determined the normal 24 h excretion of CTAB-precipitable GAG, expressed as glucuronic acid, in the urine of normal children (table II).

Table II

Normal daily urinary GAG excretion (expressed as glucuronic acid)

Age (yrs)	N	GAG-uria (glucuronic acid) µmol/24 hr	mg/24 hr
0-1	50	9,9 ± 4,6*	1,9 ± 0,9
1-3	43	14,9 ± 5,7	2,9 ± 1,1
3-5	36	21,1 ± 5,7	4,1 ± 1,1
5-7	17	17,0 ± 6,2	3,3 ± 1,2
7-9	18	26,8 ± 8,2	5,2 ± 1,6
9-11	15	24,7 ± 8,8	4,8 ± 1,7

* Mean ± SD.

In approximately 700 tests of suspect cases, we found over 80 positive cases; the range of glucuronic acid excretion being from 75-450 µmol/24 h.

The fractionation of urinary GAG

As has been previously pointed out, the excretion pattern of urinary GAG has a diagnostic meaning. Since GAG are polyanions, it is possible to fractionate a GAG mixture by means of ion-exchange chromatography. The macromolecular GAG were isolated from urine by Sephadex G-10 gel filtration along with proteins and sugars. The eluate was concentrated by means of freeze-drying.

The fractionation of the urinary GAG was done on 38 x 0,7 cm (resin bed) columns filled with Dowex 1-X2 (Cl^-) according to Varadi et al. (31), and Teller and Ziemann (32). GAG are eluted from these columns with NaCl solutions of stepwise increasing concentration. In the first fraction, proteins and free sugars are eluted along with hyaluronic acid (HA). Table III gives details on elution and nomenclature of GAG. All of the fractions were analysed for their uronic acid content by the carbazole reaction (29, 30) or by the naphtoresorcinol reaction of Pelzer and Staib (33) with minor modifications.

Table III

Elution scheme and GAG eluted

Fraction	Number of tubes	GAG eluted
0,50 M NaCl	4	HA * + proteins and sugars
1,25 M NaCl	7	Hep-S
1,50 M NaCl	7	Ch-4-S, Ch-6-S, Derm-S
2,00 M NaCl	7	Derm-S
3,00 M NaCl	7	Ker-S

* HA = hyaluronic acid, Ch-4-S = chondroitin-4-sulphate, Ch-6-S = chondroitin-6-sulphate, Hep-S = heparan sulphate, Ker-S = keratan sulphate, Derm-S = dermatan sulphate.

These analyses lead to the excretion patterns given in fig. 1 and fig. 2. Fig. 1 is an example of a Sanfilippo pattern, whereas fig. 2 is an example of a Hurler/Hunter pattern.

In addition to a normal amount of hyaluronic acid (0,5 M NaCl), there is a marked increase in heparan-sulphate (Hep-S) excretion in the Sanfilippo pattern.

In the Hurler/Hunter pattern, the excretion of Hep-S and dermatan-sulphate (Derm-S) (1,5 M NaCl and 2,0 M NaCl) is strongly increased. However, we were not able to detect differences in the excretion patterns of Hurler and Hunter patients. In concluding, for the definite assessment of the diagnosis Hurler or Hunter, the excretion patterns of urinary GAG, obtained by the methods described, cannot be used. The separation of urinary GAG on ion-exchange resin gives only information about the provisional diagnoses Sanfilippo, or Hurler/Hunter.

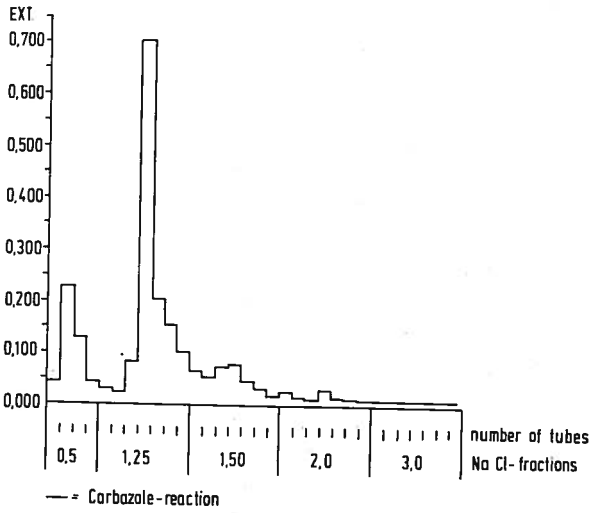

Fig. 1.
Typical excretion pattern of urinary GAG in a Sanfilippo patient. In addition to a normal amount of HA (0,5 M NaCl) a strongly increased amount of Hep-S (1,25 M NaCl) is present.

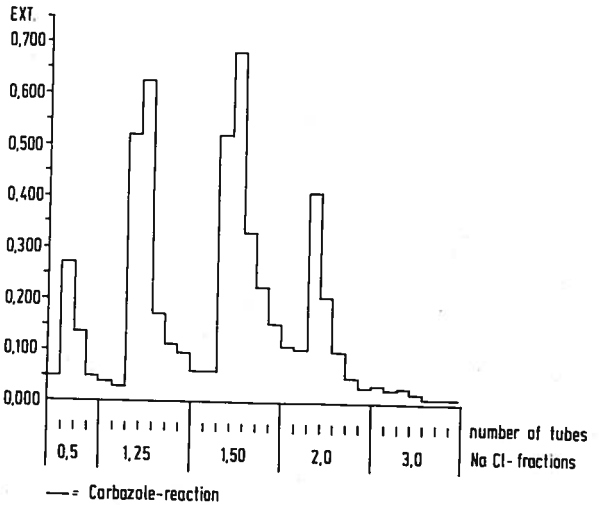

Fig. 2.
Typical excretion pattern of urinary GAG in a Hurler/Hunter patient. In addition to a normal amount of HA (0,5 M NaCl) increased amounts of Hep-S (1,25 M NaCl) and Derm-S (1,50 M NaCl and 2,0 M NaCl) are present.

Further analysis of urinary heparan-sulphate (Hep-S)

As the GAG-excretion patterns of Hurler and Hunter patients are identical and do not give information with regard to the diagnosis, we studied the chemical composition of the Hep-S fraction (1,25 M NaCl) of a group of 21 Hurler/Hunter patients. The aim of this study was to detect possible chemical differences between

Hurler and Hunter Hep-S. Heterogeneity in the chemical structure of GAG is commonly accepted nowadays (34, 35) and we expected that there might be a type-specific heterogeneity between Hurler and Hunter Hep-S.
Apart from uronic acids, aminosugars (particularly glucosamine and galactosamine) are the major components of GAG (21). As methods for the determination of glucosamine and galactosamine in GAG were already published, we started with the determination of these aminosugars in urinary Hep-S.
Hep-S (fraction 1,25 M NaCl) was hydrolysed (8 h, 100°C, 6 N HCl) and the glucosamine and galactosamine were separated by means of ion-exchange chromatography on 38 x 0,7 cm Zeokarb-225 columns according to Gardell (36). The glucosamine and galactosamine can be determined by the Elson-Morgan reaction (36, 37).
The results of this study are summarized in table IV.

Table IV

Glucosamine and galactosamine content, in % of the total hexosamine content, in urinary Hep-S of different patients.

Patients	N	Gluc. NH_2 (%-age)	Gal. NH_2 (%-age)
Hurler girls	4	64,6 ± 3,2 *	35,4 ± 3,2
Hurler boys	7	60,3 ± 3,0	39,7 ± 3,0
Hunter (boys)	10	87,4 ± 4,6	12,6 ± 4,6
Sanfilippo	21	90,0 ± 3,7	10,0 ± 3,7
Normals	11	40,0 ± 2,4	60,0 ± 2,4

* Mean ± SD.

Attention should be given to the fact that the Hunter disease is sex-linked. This means that 4 girls with a Hurler/Hunter excretion pattern must be Hurler patients.
Our group of 17 unclassified Hurler/Hunter patients, all of them boys, fell into two distinct groups. The first group of 7 boys had a glucosamine/galactosamine ratio in accordance with the Hurler girls and the boys were assumed to be Hurlers. A second group of 10 boys had a significantly different glucosamine/galactosamine ratio and these boys were assumed to be Hunters. For comparison, the same data for Sanfilippo patients and normals are given. As can be seen from the table the relative contents of glucosamine and galactosamine in Sanfilippo and Hunter Hep-S are (statistically) identical. Up to now we have only a tentative explanation for this identity, and it is obvious that these phenomena need further study.
In a number of cases, we were able to confirm the diagnosis 'Hunter' by means of pedigree studies. No conflicting data were found up to now. Radiosulphate uptake studies and corrective factor studies of fibroblast cultures are still under way (38,39).
In concluding, three criteria are used for the assessment of the exact diagnosis GAG-storage disease by means of the investigation of urinary GAG:

1. The (increased) GAG-uria is an indication of a GAG-storage disease.
2. The excretion pattern of the urinary GAG gives information regarding the diagnosis Hurler/Hunter or Sanfilippo.
3. The glucosamine/galactosamine ratio in the urinary Hep-S proves the diagnoses of Hurler and Hunter and confirms the diagnosis of Sanfilippo.

Overall results

The overall results obtained by the techniques described are listed in table V. It should be stressed that in a number of cases patients died before we were able to classify them. In other cases, it could be deduced from hospital records that sibs of patients died 'from the same disease'. These cases are also recorded in the table.

Table V

Survey of the total number of patients

Type	Total number	Investigated	From records
Hurler	21	16	5
Hunter	14	14	—
Sanfilippo	54	47	7
Not classified	5	5	—
	94	82	12

From the known ages of the patients at detection or confirmation of the disease by means of urinary GAG analysis, we calculated the mean age at detection per type of disease. The results are given in table VI and fig. 3.
As may be expected, patients are detected at an age corresponding to the severity of the symptoms. It is known that symptoms develop very early in Hurlers disease. This is reflected in a mean age at detection of 3 years and 2 months. Hunter patients were detected at a mean age of 7 years and 2 months, due to the milder symptoms of this disease. The patient of 30 yrs was the only known patient with a GAG-storage disease in all three of the groups.

As some authors (40, 41) reported that the life expectancy for Sanfilippo patients is approximately as long as for Hurler patients, the detection of 8 patients with ages between 15 and 25 yrs and of 4 patients with ages over 25 yrs was a complete surprise. These, as we called them, 'old type' Sanfilippo's were all detected in two institutes for the mentally retarded. In addition to the common röntgenologic finding of a thickened calvarium, some of these 'old type' Sanfilippo's had a persistent diarrhea and typical skin lesions on legs and arms.

A full description of these patients will be given elsewhere.

During our investigation we were able to collect data with regard to the familial incidence of these diseases in our material. These data are recorded in table VII. It should be kept in mind that our group of patients is not a random group. On the contrary, there is a strongly positive selection; the presence of a known patient in a family being one of the most strong selecting factors.

Table VI

Age at detection or confirmation of disease

Type	N	Mean age (yrs)
Hurler	16	3 2/12
Hunter < 15 yrs	13	7 2/12
Hunter > 15 yrs	1	30 6/12
Sanfilippo < 15 yrs	35	6 9/12
Sanfilippo 15 - 25 yrs	8	18 6/12
Sanfilippo > 25 yrs	4	31

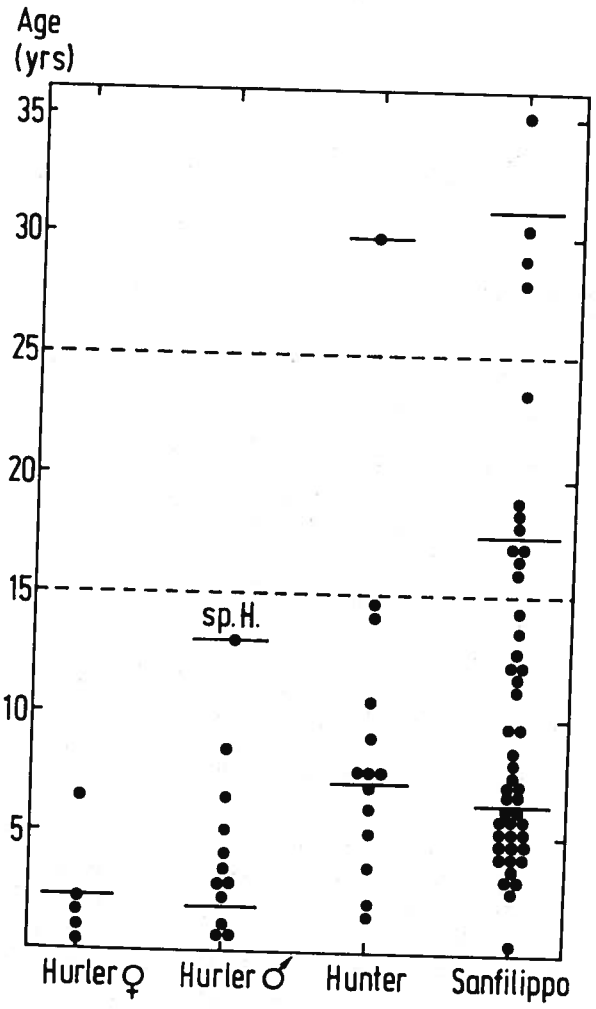

Fig. 3.
Plot of number of patients per type of disease versus age at detection (or confirmation) of diagnosis. The mean age at detection per group is given by ———

Table VII

Familial incidence of GAG-storage diseases in our material.

Type	Number of families with 1 pat.	2 pat.	3 pat.	Total number of families	Total number of patients
Hurler	12	3	1	16	21
Hunter	11	—	1	12	14
Sanfilippo	19	14	2	35	53
	42	34	12	63	88

Without doubt, as in all other cases of inborn errors, there will be marriages between heterozygotes for GAG-storage diseases with only normal and/or heterozygous children.

Estimations of gene frequencies of these diseases are seriously hampered by the relatively small numbers of patients. This is true for Sanfilippo's disease to a less extent. Exact calculations are not yet possible as the consanguinity rate in the families is not (yet) known. These data are not always correctly noted in the records, or are even not known to the parents.

However, assuming that half of the Sanfilippo patients were detected, we calculated a birth rate of 10 patients in 250,000 live births a year in this country. This leads to a reasonable estimation of the gene frequency for Sanfilippo's disease of 1 : 80 to 1 : 100.

This frequency equals the frequency of, for instance, phenylketonuria. A figure of ± 1% among institutionalized patients is given for phenylketonuria (43), and indeed we found approximately 1% of the population to be affected by Sanfilippo's disease in the institutes investigated.

For these reasons, we now believe that Sanfilippo's disease might be one of the major inborn errors

of metabolism giving rise to mental retardation. In this estimation, the occurrence of (at least) two types of Sanfilippo's disease, type A and B (6, 7), is not taken into account.
Tissue culture of skin fibroblasts offers a possibility to distinguish between these two types. Results of such studies, now underway, are not yet available. At present, no predictions can be made about the gene frequency of the A and B types of Sanfilippo's disease. The given estimation is really a simplification of the real situation and is only valid for descriptive purposes.

Antenatal diagnosis

Antenatal diagnosis of genetic diseases is widely used nowadays. Amniotic cells (cultured or uncultured), amniotic fluid, fetal skin, and even fetal blood cells, are investigated for diagnostic purposes (44). Whereas in the sphingolipidoses the lysosomal enzyme deficiencies are exactly known, in the GAG-storage diseases only a very incomplete picture of the enzyme deficiencies is available.
Enzyme studies in amniotic cells are thus of little help in GAG-storage diseases. Radio-sulphate uptake studies (45) are of far more importance. The determination of GAG in amniotic fluid has been discussed recently in the literature.
There is general agreement that the amniotic fluid originates (at least partly) from the fetal urine. However, there is some controversy as to the moment at which fetal urine production starts and at what moment fetal GAG appear in the amniotic fluid (46).
The chemical determination of amniotic GAG is very attractive because it has certain great advantages over the time-consuming culture techniques.
We are now studying GAG in normal amniotic fluid in relation to the duration of the pregnancy. Though this technique has been criticized recently (47), we believe that it is worthwhile to gather more information on the development of the normal pattern of amniotic GAG. It might even be possible to draw conclusions from the pattern of GAG in amniotic fluid (48).

Concluding remarks

There is no doubt that the role of mucopolysaccharidosis as a cause of mental retardation has been hitherto underestimated in this country. Attention should be given to non-institutionalized children and to those patients in institutes exhibiting a progressive dementia of unknown origin.
Typical skin lesions and persistent diarrhea sometimes occur in patients with Sanfilippo's syndrome (42), though (röntgenologic) thickening of the calvarium is a far more pathognomic sign. As can be seen from our data, not all patients with GAG-storage diseases die at an early age.
Compared to more elaborate cell-biological techniques (e.g., corrective factor studies and radio-sulphate uptake studies) the analysis of urinary GAG is a very rapid procedure, giving results within a few days.
Though results reported in the literature (44, 48) are not hopeful, it is worthwhile to study GAG in amniotic fluid in more detail and to see whether or not this technique is appropriate for antenatal diagnosis.

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An explorative ethological study of the social behaviour structures of a group of mentally retarded children *

F. A. Bodnár, human-ethologist
Department for child psychiatry
State University Utrecht

Summary

This preliminary report is part of a larger study, where other groups of mentally retarded children are involved. In this paper we have paid attention to the frequency analysis. Elsewhere we shall deal with sequential analyses.
As for the results of this frequency analysis they might be characterized as follows:
Compared with normal children of the same mental age, mentally retarded children display less behavioural elements that require a high degree of motor ability. In general behaviour elements when they occur have a relatively longer duration. Many elements repeat themselves, - rocking and automanipulation score extremely high on this point. Here one might speak of ritualization of behaviour. A behaviour once begun tends to survive the situation by which it was evoked. The change in behaviour is more sluggish than the change in situation.

Introduction

Ethology has developed out of Zoology. It deals with the study of the behaviour of the organism and is characterized by the use of strict quantitative methods. So it is not concerned with information obtained by means of introspection and empathy.
The problems of ethology can be reduced to five key-questions:

1. What behaviours does the species have? (the morphological analysis)
2. What are the causes of their appearance? (the causal analysis)
3. What is their function? (the functional analysis)
4. How has this behaviour developed in evolution?
5. How has this behaviour developed in the life of an individual?

Morphological analysis (description)

Behaviour is a continuous stream of movements and postures. In the first stage of the ethological study this stream is broken up into its more or less stereotype invariant elements. Element is understood as the smallest possible invariant behaviour-unit which is still relevant within the scope of a particular study. This molecular approach is necessary to guarantee the greatest possible objectivity. Later syntheses can then be based on empirical categorisations.
When an ethologist examines a species he will start with the study of the total behaviour of that species in its natural environment so that recurrent elements can be discovered and defined.
With higher developed species of animals the complexity of their behaviour clearly increases, partly as a result of greater motor possibilities of the organism, partly as a result of an increased flexibility in the composition of motor patterns.
In a study of jumping-spiders the majority of behaviour variations could be discribed with some 15 elements, whereas the study of the chimpanzee's social behaviour required at least 64 elements (Van Hooff, 1971).

Causal analysis

The various elements of behaviour do not appear at random. On the contrary, there is a certain coherence in the appearance of the behaviour elements. When elements of behaviour occur closely together in time this means either that they have common causes or that one element brings about the next.
The factors which determine the appearance of a behaviour can be roughly differentiated into:

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