Antenatal Development of Amylase Isoenzymes

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Relatively little is known about the normal physiology of amniotic fluid, its dynamics, and its constituent enzymes and isoenzymes.

The antenatal diagnosis of some metabolic errors is frequently based upon the investigation for the presence or absence of an enzyme in the amniotic fluid or cells. In establishing an antenatal diagnosis of this kind, it is essential that 2 major factors be borne in mind:

1. During fetal development and, indeed, during the first months of life, an enzyme may not be present in normal circumstances and its absence is of no prognostic or diagnostic value.

2. If an enzyme is present at fetal development, it may only be represented by some of its isoenzymatic forms, not by its phenotypical appearance and function as recognized later in life. This can influence, both quantitatively and qualitatively, a prenatal diagnosis, possibly in the wrong direction.

The purpose of the present study was to investigate the dynamics of such an enzyme, namely, of alpha-amylase (alpha-1, 4-glucan 4 glucanohydrolase) during fetal development, by subjecting amniotic fluid at various stages of pregnancy to the electrophoretic technique used for amylase detection and separation.

Previous studies have revealed the presence of 2 polymorphisms controlled by 2 (possibly 3) loci—one controlling pancreatic amylase secretion and the other salivary amylase secretion. Other previous investigations, based on the study of 100 infants, followed monthly from birth to 12 months, have shown that, postnatally, pancreatic activity develops more slowly than salivary activity and the complete phenotype, as observed in the electrophoretic pattern of serum or urine of older children and adults, is not usually present until approximately the 12th to 14th month of life. The curve of development of each fraction, with age, is demonstrated in Fig. 1 (Kamaryt and Fintajslova, 1971).

Both polymorphisms are easily detectable and qualitatively identical in the serum and urine of mature individuals. Since fetal urine probably constitutes a major part of amniotic fluid, it was assumed that it should represent a suitable medium for the antenatal detection of both these polymorphisms.

Materials

Forty specimens of amniotic fluid† (collected for various other reasons) were investigated and the observed isoenzymatic variants compared with corresponding specimens of maternal urine. The stages of pregnancy at which transabdominal amniocentesis (and collection of urine) was performed are shown in Table I. All specimens were investigated, within 4 days of collection, by the standard electrophoretic technique.

Results

1. No amylolytic activity was detectable in amniotic fluid before, or during, the 12th week of pregnancy, i.e., in 7 out of 40 specimens.

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† I am indebted to Mr Victor Lewis of Shroddells Maternity Unit, Watford for the majority of these specimens.
TABLE I

<table>
<thead>
<tr>
<th>Stage of Pregnancy (wk)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of specimens</td>
<td>6</td>
</tr>
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</table>

* The 25–26 weeks specimen and urine were repeated at full term and identical results obtained.

(2) In all specimens where activity was detected (33 out of 40), only one of the polymorphisms was present, namely that representing the salivary locus —migrating more slowly from the anode (Fig. 2).

(3) Two of the 33 specimens (6%) were characterized by the heterozygous 2-band Amy 1A1B variant (see Fig. 3 where the record obtained from the amniotic fluid is compared with that from the maternal urine). The remainder were of the one-band Amy 1A1A homozygous type (as demonstrated in Fig. 2).

(4) No pancreatic amylolytic activity was observed in any of the specimens of amniotic fluid investigated, though all maternal urines had typical findings with both polymorphisms present.

(5) In two of the maternal urine specimens, amylolytic activity was found to be considerably raised.

One specimen had been collected from a diabetic mother, the other from a mother who had a severe antepartum, and subsequent postpartum, haemorrhage.

**Discussion and Conclusions**

(1) None of the amylase isoenzymes appears to be developed in amniotic fluid before the 12th week of pregnancy.

(2) After the 12th week of pregnancy, amylase activity is represented by the salivary locus only, the pancreatic locus does not seem to be active. This is in agreement with previous observations of the development of both fractions during the first 12 months of life.

(3) Two out of 33 specimens (6%) had the heterozygous, 2-band Amy 1A1B phenotype. The sample is small but this is the expected frequency, corresponding to that in the general population, where this particular phenotype has been observed in 7%.

(4) The absence of pancreatic isomylase from all 33 specimens seems to suggest that they all consisted of exclusively fetal material, since no healthy, mature individual has as yet been observed to lack pancreatic amylase. Consequently, this may prove
to be a useful technique which would facilitate
differentiation between fluid of maternal and fetal
origin.

(5) A quantitative increase in amylase activity in
prenatal specimens of maternal urine may prove to
be of pathological significance (eg, in diabetes).

(6) The pancreatic locus has now been definitely
assigned to chromosome No. 1 by the finding of
linkage between Amy 2 and the 'uncoiler' pheno-
menon (Un-1) by Kamarýt, Adámek, and Vrba
(1971); by the original discovery of linkage between
Duffy and congenital cataract Cae by Renwick
and Lawler in 1963; the subsequent report of
linkage between Duffy and Un-1 by Donahue et al
(1968); and the recent confirmation of linkage be-
tween Amy 2 and Duffy by Hill, Rowe, and Lovrien
(1972). Preliminary studies on data from one
family (Laxova, 1968) showed that both amylase loci
were probably linked.

Since the salivary locus, which is identifiable
antenatally, is also on chromosome No. 1, it may
eventually prove useful for future antenatal linkage
studies in a limited number of indicated cases,
possibly also in connection with the early detection
of congenital cataract.

Summary

The two types of the amylase polymorphism,
which are controlled by the salivary and pancreatic
loci respectively, do not appear in their permanent
form, in the serum or urine, until after the 2nd year
of life.

The development of the isoenzymes has been
investigated electrophoretically in a series of
samples of amniotic fluid collected at various stages
of pregnancy and compared with the isoamylases in
the maternal urine. It seems that, antenatally,
only the salivary polymorphism is active. After the
12th intrauterine week it may be detected in both its
homozygous and less frequent heterozygous forms.
Since the amylase loci have now been assigned to
chromosome No. 1, these findings may eventually
prove useful for antenatal linkage studies in indi-
cated cases.

Addendum

Since the preparation of this paper, evidence for
close linkage between the two loci has been sub-
mitted for publication by A. D. Merritt, Marian L.
Rivas, and J. G. Ward (personal communication).

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for technical assistance.

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