striatal tissue shows the latter to be 5–10% of the former. As DOPAC is presumably an intraneuronal metabolite[13], its concentration in striatal dopaminergic nerve endings would be 400–800 μg/g, which is roughly equivalent to $2–4 \times 10^{-3}$ *M*, if 1 g of wet tissue is set equal to 1 ml of liquid. This concentration coincides with the threshold inhibitory concentration of DOPAC shown in the Figure.

Considering that neuroleptics increase the concentration of endogenous DOPAC enormously, it seems possible that the antipsychotic activity of these drugs is related to the rise in the intraneuronal content of DOPAC acting as a methylation regulator. This implies that the methyltransferase is localized intraneuronally. The calculation above is based on data from striatal dopaminergic neurones. There are no corresponding data available on other central dopaminergic neurones, but also no evidence to indicate that they differ very much in this respect.

Thus, the regulation mechanism outlined above is not necessarily restricted to striatal neurones. High concentrations of 5-MTHF and high activity of tryptamine-N-methyltransferase were in fact detected in rat corpus striatum, but considerable amounts and activities have also been found in other brain regions[14,15]. Tryptamine is certainly not the only substrate of this enzyme leading to the formation of psychotomimetic derivatives. Other indoleamines, for instance, such as bufotenin or 5-methoxy-N,N-dimethyltryptamine[6], and catecholamines[1] also, have been held to be possible psychotogenic substances.

It is not yet definitely known whether biogenic amines do in fact serve as 'precursors' of endogenous psychotogenic substances, much less which particular amine might be specifically concerned. Should dopaminergic neurones be involved, then it may be assumed that DOPAC fulfils a regulatory function.

Résumé. L'acide dihydroxyphénylacétique (DOPAC) et l'acide homovanillique (HVA) inhibent la méthylation de la tryptamine par une méthylase partiellement purifiée du cerveau de rat. Les concentrations nécessaires à cette inhibition sont hautes et du même ordre de grandeur que celles qu'on peut attendre du métabolisme de la dopamine au niveau des terminaisons dopaminergiques. La chlorpromazine et la clozapine n'influencent pas cette activité enzymatique.

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Feto-Specific Features of Human β_2-Microglobulin

Ontogenetic studies on plasma proteins showed that the concentration of individual proteins gradually increases with the maturation of the fetus. Some proteins reach the adult levels already during the intrauterine life, the concentration of others raises slowly and the adult levels are attained later in the extrauterine life. An exceptional developmental pattern is presented by feto-specific proteins[1] (e.g. α-fetoprotein, fetuin) that reach the highest concentrations already during the fetal period and the levels attained are higher than those found in healthy adults. Some of these proteins almost disappear from the sera after birth and can only be detected by highly sensitive techniques such as radioimmunoassay.

We have studied the ontogenesis of human β_2-microglobulin, a low-molecular-weight constituent of human serum and other body fluids[2]. This protein has been shown to be homologous to the constant domains of immunoglobulin G light and heavy chains[3], and to be produced in vitro by lymphoid cells as well as by a variety of cells derived from non-lymphoid solid tissue lines[4–7]. The present study demonstrates the presence of β_2-microglobulin in fetal sera and other fetal fluids; the concentration changes of this protein in serum during fetal development were found to be similar to those of feto-specific proteins.

Materials and methods. Human fetuses of 16 to 36 weeks of gestation were obtained from spontaneous or Cesarean abortions; the gestational ages were estimated according to the last menstrual date, the body weight and the crown-heel length. Fetal urine was obtained by needle aspiration after exposure of the bladder by dissection. Amniotic fluids were taken in connection with diagnostic amniocenteses. All samples were kept frozen at −20 °C until used.

β_2-Microglobulin was quantitated by the radioactive single radial immunodiffusion method as described earlier[8]; antisera against β_2-microglobulin were raised in rabbits by immunization with purified antigen isolated from urine of kidney transplant patients[9].

Results and discussion. β_2-Microglobulin was detected in all fetuses investigated. The concentration of the protein in fetal sera was found to be considerably higher than in normal adult sera; the mean value for the fetal sera studied was 0.71 mg/100 ml (range 0.28 to 1.36 mg/100 ml) as compared to adult serum values ranging from 0.11 to 0.24 mg/100 ml (ref. [8]). The change in β_2-microglobulin concentration with the gestational age is shown in the Figure. The highest concentrations were found in fetuses between the 20th and 32nd weeks of gestation; at the end of the second trimester the level of β_2-microglobulin was approximately 8 times higher than the mean concentration found in sera of healthy adults. After this period, the concentration of the protein decreases to reach the levels of cord blood sera (range 0.20 to 0.48 mg/100 ml). Relatively high concentrations of β_2-microglobulin were also found in fetal urines and amniotic fluids. In 5 urine specimens from 16- to 36-week-old fetuses the β_2-micro-

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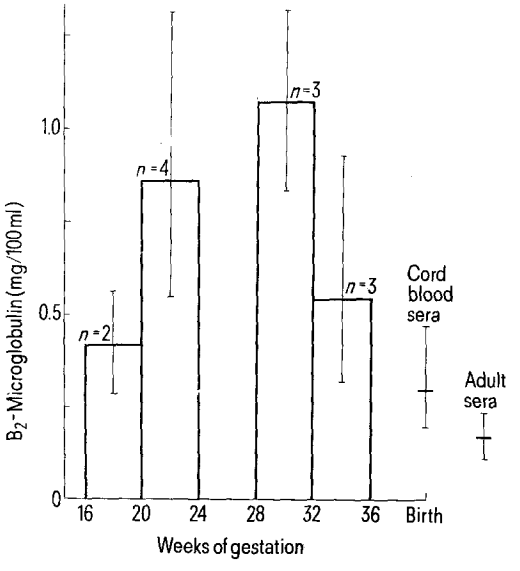
globulin concentration ranged from 0.18 to 0.55 mg/100 ml. In 37 samples of amniotic fluids from pregnant women of different gestational ages the concentration of the protein ranged from 0.12 to 1.80 mg/100 ml.

β_2-Microglobulin present in fetal sera may be of fetal as well as of maternal origin. A possible transplacental passage of β_2-microglobulin from the maternal to the fetal circulation was not investigated in this study; however, β_2-microglobulin concentration in sera of 84 pregnant women of different durations of pregnancy was found to be within the range of normal adult levels. On the other hand, there is strong evidence that the human fetus is capable of autonomous synthesis of β_2-microglobulin; we found that kidney, liver, thymus and testis tissues of a 16-week-old fetus incorporated ^{14}C-labelled amino acids into β_2-microglobulin in tissue cultures. In addition, our experiments with established cell lines from fetal lung, skin and from cord showed that the fetal cells are able to release β_2-microglobulin into culture medium. Whatever the source of the protein in fetal sera, its concentration changes during the fetal life present β_2-microglobulin as a protein with feto-specific features.



Dependence of fetal serum β_2-microglobulin on gestational age.

Feto-specific proteins are known to occur at increased concentrations in sera of patients with certain malignant diseases. β_2-Microglobulin seems to present similar features: in a large group of patients studied by Evrin and Wibell[10] the majority of patients with increased β_2-microglobulin concentration suffered from malignant diseases. Also in our survey of patients with malignant disorders a high percentage of these patients showed increased β_2-microglobulin levels as compared to patients with non-malignant diseases. This increase was particularly pronounced in multiple myeloma (80% of patients), carcinoma of stomach (57%), cervix and uterus (54%) and carcinoma of breast, lung and colon (40%). Since the biological function of β_2-microglobulin is not known at the present time, we can only speculate on the relationship between its feto-specific features and increased concentration in some neoplastic diseases.

Zusammenfassung. Im fötalen Blut erreicht die Konzentration von β_2-Mikroglobulin in der 30. Schwangerschaftswoche ihr Maximum. Im mütterlichen Blut tritt während der Schwangerschaft kein Konzentrationsanstieg auf. Hingegen wurden bei Erwachsenen mit verschiedenen malignen Tumoren erhöhte Serumkonzentrationen beobachtet.

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A New Pyroglutamylpeptide (Pyr-Lys-Ser) Isolated from the Venom of *Agkistrodon halys blomhoffii*

Five bradykinin-potentiating peptides (potentiators A, B, C, D and E), which potentiate specifically the actions of bradykinin, were isolated from the venom of *Agkistrodon halys blomhoffii*, and the amino acid sequences of three of them were determined successfully with the combined method of Edman degradation and mass spectrometry[1,2].

During the course of the mass spectrometric investigation on the structures of these peptides, it was found that some preparations were contaminated with a small amount of unknown peptides[2]. Further purification was achieved by passing the preparations through a Dowex 50×2 column instead of CM-Sephadex C-50 column previously employed, and potentiator A was separated from the contaminating peptides and determined to be Pyr-Gly-Arg-Pro-Pro-Gly-Pro-Pro-Ile-Pro[3].

The present paper describes the chromatographic isolation of a new peptide (I) and its amino acid sequence, which was determined by mass spectrometry and confirmed by chemical synthesis.

A pool of the minor peptide mixture, which was eluted from a Sephadex G-25 column later than the potentiating peptides[1], was applied on a Dowex 50×2 column equilibrated with 0.05 *M* pyridine-formic acid buffer, pH 3.1. (I) was eluted between potentiators A and E with the same buffer, and about 7 mg of the material were obtained from 10 g of the venom.

Acid hydrolysis of the sample by constantly boiling HCl yielded equimolar amounts of glutamic acid, serine and lysine (Glu 1.0, Ser 0.8, Lys 0.7), and it had no free N-terminal residue, as in the cases of potentiators A, B, C and E, when detected by Edman degradation. (I) was

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