

plexes similar to those in the basic selenate to be present in the unit cell according to the symmetry $P2/n$. Three dimensional Fourier maps seem to confirm this assumption and also reveal the positions of four of the sulfate groups in a fourfold position; the remaining two sulfate groups, however, are apparently statistically distributed over two positions close to a center of symmetry in the unit cell. This result in connection with the fact that for some of the zonal data, for example the $h3l$ -reflections, the intensity distribution is closer to one expected for a noncentrosymmetric space group seems to indicate the presence of small deviations from a centrosymmetric arrangement. The space group should then be Pn rather than $P2/n$. The refinement of the structure will be continued according to this space group.

The reliability index, R , assuming the space group to be $P2/n$, is at the present stage of the refinement 0.24 for all observed reflections. The parameters for the aluminium atoms in the aluminium-oxygen complexes are:

Atom	Parameters		
	x	y	z
4 Al ₁ :	0.338	0.980	0.220
4 Al ₂ :	0.482	0.796	0.267
4 Al ₃ :	0.137	0.795	0.390
4 Al ₄ :	0.307	0.437	0.329
4 Al ₅ :	0.276	0.620	0.437
4 Al ₆ :	0.453	0.619	0.375
2 Al ₇ :	1/4	0.705	1/4

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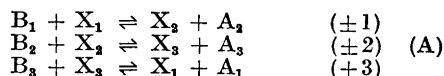
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On Observable Discontinuities and Coherence in the Kinetics of Enzymically Reacting Systems. A Misprint

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The following misprint in my paper in this volume p. 107 should be corrected: The sequence (A) should read



X_1 , X_2 and X_3 being three different forms, or compounds with the substrates (B_i , A_i), of the enzyme. The plus signs mean the reactions in the direction from left to right, the minus signs indicating reactions in the opposite direction.

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Free Butyric Acid as a Possible Source of Off-Flavour of the Cow's Milk After Administration of Oestrogens

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During investigations on the metabolism of oestrogens in the cow undertaken at this department¹ peculiar alterations of the milk after parenteral administration of the hormones were repeatedly observed². To further explore the nature of these alterations 10 mg oestradiol-17 β in 5 ml propylenglycol was injected intramuscularly to a non-pregnant cow producing 8 liters milk a day. Daily milk samples were frozen on the day of drawing and analysed in series immediately after thawing.

On the week after injection the milk produced per day gradually decreased to

5 liters and showed a strong ability to foam when stirred. The most striking change in the milk was the development of an acid, nauseous taste.

The following milk constituents were determined: sodium and potassium (flame photometry of trichloroacetic filtrates), calcium and magnesium (flame photometry after resp. oxalate and ammoniumphosphate precipitation), chloride (flame photometry after silver precipitation), lactose (polarimetry), fat (Gerber), citric acid (heating with acetic anhydride and pyridine) and free fatty acids (titration of ether-petroleum ether extracts³).

The maximal deviations were found to occur on the third day after injection when sodium had increased to 22 mequiv/l (from 15 mequiv/l), chloride to 42 mequiv/l (from 27 mequiv/l) and potassium decreased to 27 mequiv/l (from 38 mequiv/l) indicating a decreased diluting resp. concentrating ability of the mammary gland. At this time calcium had increased to 63 mequiv/l (from 40 mequiv/l), and fat to 5.5 % (from 3.8 %). A few determinations (biuret method) indicated increased protein content. The other constituents analysed showed minor variations in concentration except the extractable fatty acids which had increased 30-fold (see Table 1).

A sample of the milk drawn on the third day after injection was acidified with concentrated phosphoric acid, extracted 3 times with its equal volume of ether and the extracts titrated. After re-acidification the samples were submitted to gas liquid partition chromatography⁴ for identification and titration of volatile fatty acids. In each of the three extracts butyric acid corresponding to about 10 % of the titre of the extracted acids was found and the total amount of butyric acid in the milk sample was roughly estimated to 1 g/l. No other volatile acids could be found.

It was therefore suspected that the butyric acid could be responsible for the off-flavour of the milk. This was substantiated by the strong aggravation of the off-flavour following acidification of the milk with mineral acids and by organoleptic comparison with normal milk to which butyric acid had been added.

Small increments of the free fatty acids were also found in connection with the two following natural heats and after an injection of 10 mg oestrone, but no corresponding off-flavour of the milk was perceptible. Injections of various oestrogens to 8 cows

Table 1. Titrable acidity in ether-petroleum ether extracts of milk³ after administration of oestrogens and during heats. Consecutive days.

ml 0.01 N NaOH per 10 ml milk.	Remarks.
1.0	
1.4	
0.9	10 mg oestradiol-17 β .
10.0	
26.0	
30.2	
18.2	
10.5	
5.3	
2.2	
0.8	} Heat.
0.8	
2.0	
1.3	
0.7	
0.7	
0.7	
0.5	10 mg oestrone.
0.7	
1.9	
2.5	
2.5	
—	Sample lost.
1.5	
1.2	
1.0	
0.6	
0.6	
0.7	
1.0	
1.5	} Heat.
2.5	
5.2	
4.0	
2.5	
1.5	
1.2	

in high yield (between 1 and 2 months after parturition) did not alter the concentration of free fatty acids of the milk.

It is a clinical experience that cows suffering from cystic ovaries may secrete an off-flavoured milk with a salty and bitter taste⁵. From the above described findings in the milk following parenteral administration of oestrogens and in connection with heat it seems justified to ascribe this milk abnormality to an altered oestrogen status of the cows. The stage of the lactation period seems, however, to be of importance. Milk of this kind, presumably with a high

lipase activity⁶, may render large amounts of normal milk unpalatable when admixed prior to processing for consumption.

More systematic investigations are in progress.

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The Fatty Acid Composition of Cerebrospinal Fluid Lipids

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The study of the fatty acid composition of the different lipids of human cerebrospinal fluid (CSF) has not previously been possible due to the lack of suitable analytical methods which could be applied to the small amounts of lipid available. The CSF contains only 1-1.5 mg of total lipids¹ per 100 ml and ultramicrochemical techniques have to be applied to normal and abnormal fluids if neurochemical correlations are to be made. Through the use of the technique described below it has been possible to identify the fatty acid pattern of cholesterol esters, glycerides and phospholipids of normal human CSF.

Pooled normal CSF (140 ml) obtained from individuals without neurological symptoms was used for the analysis. The CSF was immediately centrifuged after lumbar puncture, the cell-free supernate was carefully removed and aliquots taken for determination of total protein. The rest of it was kept at -20°C until analyzed. All specimens used had normal white cell count and normal protein concentrations. The pooled CSF was concentrated by dialysis in a collodium bag under reduced pressure according to Mies² and extracted with 20 volumes of chloroform:methanol 2:1 and washed with water³. The total lipids (1.8 mg) were separated on a silicic acid column⁴ (0.2 g) into cholesterol esters, glycerides + free fatty acids and phospholipids. The different lipid fractions were hydrolyzed and the fatty acids were isolated after saponification and acidification. The fatty acid composition was defined by gas-liquid chromatography according to James and Martin⁵ using an Argon Pye chromatograph with an ionization chamber as detector. Because of the complexity of the fatty acid pattern, it was necessary to chromatograph the mixed methyl esters on two different stationary phases, a polar polyester (LHC-R-296)⁶ and silicone oil. In addition chromatograms were obtained on the mixed esters after complete hydrogenation in order to obtain an accurate chain-length analysis. The analytical procedures used otherwise have been described earlier.⁷

The determination of the fatty acid composition of the different lipid components of human CSF is summarized in Table 1. For comparison the fatty acid composition of the different lipid classes of normal serum is also included in the table. Three characteristic fatty acid patterns are found in the cholesterol esters, glycerides + free fatty acids and phospholipids of human CSF. The fatty acid composition of the CSF resembles the serum lipids, but there are certain differences. Especially remarkable is the very low concentration of linoleic acid in the cholesterol esters of CSF compared with that of the serum cholesterol esters. Another interesting finding is the rather high concentration of palmitoleic acid in the glycerides + free fatty acid fraction and in the cholesterol esters. In the group C₂₀₋₂₂ several peaks were found among the phospholipid fatty acids. Significant amounts of a fatty acid with 24 carbon atoms were also found in the phospholipids of the CSF. Work is in progress to identify these fatty