posure, and this was not attended by a marked alteration of its chronotropic effect.

Hence, the data of our experiments on the simulation of acute and subacute circulatory failure and in isolated myocardial preparations indicate certain differences in the effects of antiarrhythmic drugs with different mechanisms of action on the toxic, cardiotonic, and chronotropic effects of strophanthin. In contrast to trimecaine, ajmaline greatly increased the resistance of a weak heart to strophanthin cardiotoxicity under conditions of simulated circulatory failure. On the other hand, both antiarrhythmic agents somewhat attenuated the cardiotonic effect of cardiac glycosides, and this should be borne in mind when prescribing combinations of these drugs. Evidently, clinical use of ajmaline in combination with cardiac glycosides is preferable to combinations with trimecaine, particularly so if manifest symptoms of the toxic effects of glycoside cardiotonics are to be eliminated.

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MICROBIOLOGY AND IMMUNOLOGY

The "Familial" Factor and the Microbiocenosis of the Normal Human Intestine

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Population genetics methods are used to study the relationship between living in the same environment and the formation of the large-intestine microflora in healthy persons. The variability of a microbiological phenotype is found to depend mainly on random factors and is virtually unrelated to the "familial" constituent.

Key Words: *familial analysis; normal microflora*

It is well known that people in close communal contact are frequently characterized by a certain similarity of the large-intestine microflora. It could hardly be disputed that this regularity is to a great extent explained by shared living conditions, primarily of a social nature. Nevertheless, this a

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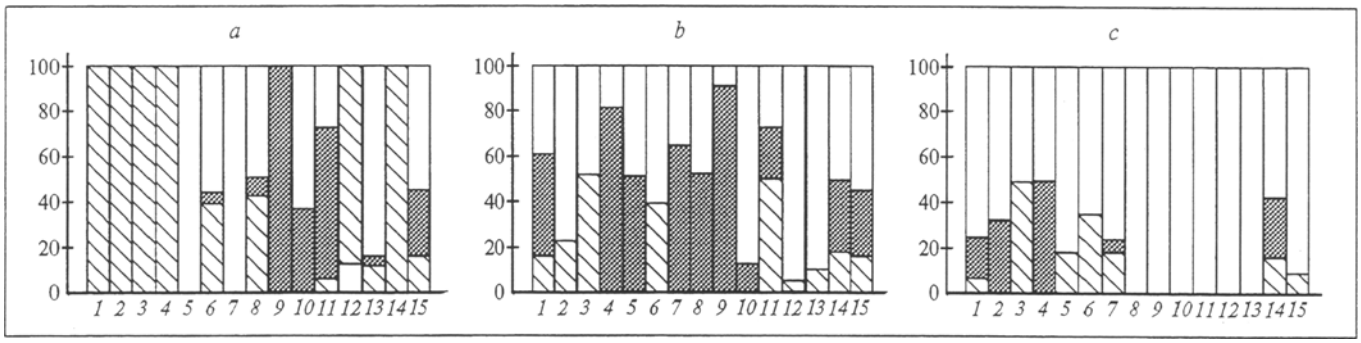

Fig. 1. Contribution of the "familial" factor to the variability of intestinal microbiocenosis parameters at the level of genus. *a*) detection frequency: *b*) quantity; *c*) specific share. General phenotypic variance components: cross-hatched bars: phenotypic, dark bars: "familial," white bars: random. Abscissa: *1*) *Bifidobacterium*; *2*) *Lactobacillus*; *3*) *Enterococcus*; *4*) *Escherichia*; *5*) *Candida*; *6*) *Clostridium*; *7*) *Staphylococcus*; *8*) *Citrobacter*; *9*) *Hafnia*; *10*) *Enterobacter*; *11*) *Pseudomonas*; *12*) *Klebsiella*; *13*) *Proteus*; *14*) indigenous bacteria; *15*) transitory bacteria. Ordinate: specific contribution of a factor, %.

priori assumption is insufficient for a correct judgment of the role of this factor in the formation of a human microbiological phenotype. In this connection we thought it interesting to quantitatively assess the effect of living in the same surroundings (e.g., a family unit) on the formation of the microbiocenosis of the large intestine of a healthy person. Methods of microbiological and population genetics analysis were used.

MATERIALS AND METHODS

Data of microbiological examinations of ten complete families (father, mother, two children, and immediate relatives) were used in this research. A total of 50 subjects aged 7 to 75 were examined, 60% of them women. At the time of the study all family members were clinically healthy without clinical or laboratory signs of disorders in the intestinal microflora.

Qualitative and quantitative examinations of the intestinal microflora were carried out as described previously [2]. The isolated cultures of opportunistic *Enterobacteriaceae* were identified by biochemical characteristics using Enterotest-1 and Enterotest-2 test systems (Czechoslovakia). The content of the isolated microorganisms (colony-forming units, CFU) was expressed as common logarithms (log CFU/g) or as their specific weight (percent concentration).

The data were statistically processed [4]. Familial analysis was carried out as a variant of twin analysis [3]. The contribution of the genotypic (G) and paratypic (E) constituents of the total phenotypic variance of traits was assessed. The latter was differentiated to the random component Ew and the effect of living within a single environment (that is, in the same family), or the "familial" factor (Ef). The relationships within the groups of compared individuals were assessed by the coefficient of intrapaired correlation [1].

The effect of the "familial" factor was estimated by the formula:

$$Ef = \frac{rPP - rS}{1 - rS},$$

where rPP is parent-parent, rS is parent-random subject. The effect of a random environmental component was calculated as Ew = E - Ef.

RESULTS

Bacteriological examinations of feces of the subjects under study demonstrated abundant microflora in the intestine (Table 1). *Bifidobacterium*, *Lactobacillus*, *Enterococcus*, and *Escherichia* occurred in 100% of cases. Staphylococci, clostridia, citrobacteria, and *Candida* fungi were isolated less frequently, but still quite often. The same bacteria predominated in the feces by weight. The greatest share in the studied microbiocenosis belonged to *Bifidobacteria*, *Escherichia*, *Enterococcus*, and *Staphylococcus* were also rather numerous. The other tested genera of microorganisms were detected in less than 50% of cases, and their quantitative parameters were much lower.

We attempted to assess the liability of the qualitative and quantitative characteristics of the microflora of the normal human intestine to paratypic factors and tried to determine the strength of the effect of the "familial" component.

Figure 1 shows that the incidence of indigenous microorganisms in the microbiocenosis was absolutely unrelated to the effects of the environmental variance of the total phenotypic variance. This fact once again confirms the notion that indigenous bacteria are an obligatory component of the normal human microflora. On the other hand, for transitory microorganisms the effects of paratypic factors were on the whole of absolute significance. These factors were mainly represented

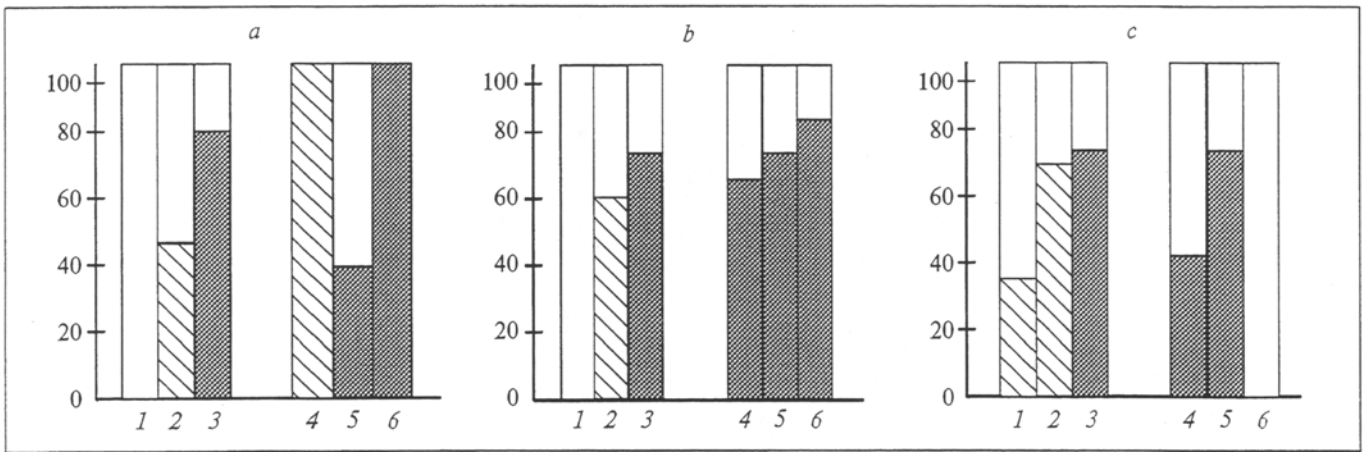

Fig. 2. Contribution of the "familial" factor to the variability of intestinal microbiocenosis parameters at the level of species and biological variant. Abscissa: *1*) *S. aureus*; *2*) *S. epidermidis*; *3*) *S. saprophyticus*; *4*) *E. coli* with normal enzymatic properties; *5*) *E. coli* with reduced enzymatic properties; *6*) lactose−negative *E. coli*. Other notation as in Fig.1.

by a random component, which surpassed the familial one by 2.6 times ($p<0.05$). Meanwhile the effect of living in the same surroundings proved to be extremely significant for the isolation rate of *Hafnia* and *Pseudomonas*.

Analysis of the quantitative parameters of the examined biotope showed that despite the significant value of the paratypic variance, the concentrations of both transitory and indigenous genera of microorganisms were on the whole little subject to the familial factor. However, this vector of variability determined to a great extent the differences in the absolute counts of *Escherichia*, *Staphylococcus*, and *Hafnia*.

Variability of the specific content of components of the large-intestine microbiocenosis was due mainly to the nonhereditary constituent, which was chiefly represented by the random variance. The data were statistically reliable ($p<0.01$). The only exception was *Escherichia*: in this case the effects of random factors were counterbalanced by the effect of living in the same environment.

These data were obtained only for genera of microorganisms, prompting speculation about the effect of the examined factor on bacteria referred to a lower classification level. To resolve this, we selected at random two genera of microorganisms of the group of transitory and indigenous bacteria, *Staphylococcus* and *Escherichia*, and identified their specific representatives. The following species of staphylococci were identified: *S. saprophyticus*, *S. epidermidis*, and *S. aureus*. Investigating *Escherichia*, we determined *E. coli* biovariants by the capacity to utilize lactose, that is, *E. coli* with normal and reduced enzymatic characteristics and lactose-negative *E. coli*.

Our data indicate that the presence of *S. epidermidis* in the intestinal microbiocenosis was mediated by the virtually identical effects of the individual genotype and environment. The incidence of *E. coli* with normal enzymatic properties was liable to change under the influence of the environmental component. In the remaining cases the paratypic factor was of paramount importance. Moreover, the presence of lactose-negative *E. coli* and *S. saprophyticus* in the microflora was largely due to living in the same quarters, whereas carriership of *E. coli* with reduced enzymatic characteristics and of *S. aureus* was a random event (Fig. 2).

A somewhat different picture emerged for the quantitative parameters. The "familial" factor proved to play an important role in maintaining the concentrations of *S. saprophyticus* and all the examined *E. coli* biovariants. The same is true about the percent content of these bacteria. However, the absolute level of *S. epidermidis* depended on the counterbalancing effect of the genotypic and random environmental factors. The absolute and relative content of *S. aureus* and the specific share of lactose-negative *E. coli* were a function of random factors.

Hence, we obtained new data on the effect of common living quarters as a mechanism contributing to the formation of a healthy person's microbiological phenotype. We revealed, first, that diverse factors of nonhereditary variation influence the formation and maintenance of transitory microflora, in contrast to indigenous microflora, in a particular healthy individual's biotope. The systematic component, presenting as the "familial" factor, and the random constituent which predominates can be clearly differentiated. This evidently means that the qualitative similarity of the allochtonous component of the bacterial picture in members of the same family has little to do with

TABLE 1. Variation Parameters of the Microbiocenosis of the Large Intestine in Examined Subjects (mean±SEM)

Microorganism	Frequency, %	Quantity, log CFU/g	Specific weight, %
Bifidobacterium	100.0	8.72±0.25	46.62±5.45
Lactobacillus	100.0	6.60±0.14	2.83±1.77
Enterococcus	100.0	7.37±0.33	16.32±3.94
Escherichia	100.0	7.82±0.24	16.57±3.80
Candida	82.0	5.36±0.41	2.17±0.94
Clostridium	72.0	4.32±0.46	2.21±1.49
Staphylococcus	96.0	6.05±0.35	7.04±2.76
Citrobacter	56.0	1.79±0.32	0.00±0.00
Hafnia	10.0	0.43±0.22	0.00±0.00
Enterobacter	24.0	1.11±0.32	0.00±0.00
Pseudomonas	46.0	2.42±0.45	2.98±2.20
Klebsiella	32.0	0.93±0.27	0.47±0.47
Proteus	16.0	0.48±0.19	0.02±0.02
Indigenous	100.0±0.00	7.63±0.51	20.59±10.68
Transitory	42.0±9.72	2.16±0.69	1.35±0.69
S. aureus	22.0	1.49±0.42	18.11±5.6*
S. epidermidis	48.0	3.13±0.53	44.17±7.17*
S. saprophyticus	34.0	2.17±0.46	33.47±6.88*
E. coli norm.	96.0	7.47±0.34	90.77±3.89*
E. coli red.	18.0	1.19±0.38	8.70±3.77*
E. coli lact.	16.0	0.91±0.31	2.64±2.07*

Note. *E. coli* norm. – with normal, *E. coli* red. – with reduced enzymatic properties, *E. coli* lact. – lactose–negative. Asterisk: reliable ($p<0.05$) differences within genera.

similar nutrition, habits, traditions, etc., that is, everything that constitutes the notion of "lifestyle." Second, it was found that the variability of quantitative characteristics of the examined genera of microorganisms, both transitory and indigenous, is also due mainly to effects of random paratypic factors. At a lower level of classification of the examined microflora of the large intestine the effect of the "familial" constituent was less evident. It was quite clearly seen in the case of *S. saprophyticus* and the absolute concentration of all the identified *E. coli* biovariants.

These results may be easily explained. People living together in a family and coming in close contact with each other in everyday life may exchange microorganisms. One may imagine that the circulation of certain microorganisms among the members of a small collective body is mediated by orofecal mechanisms with an alimentary route of transfer. But it is impossible to imagine that every individual leaving this narrow collective will be exposed to the same environmental effects. Every second the human organism is exposed to a great number of random factors which *in toto* overpower the "familial" factor. That is why our conclusion that the formation of a microbiological phenotype in a member of a closed unit results from random events is well grounded.

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