face glycosaminoglycan. We also found that sodium pentosanpolysulfate prevented the adherence of calcium and protein to bladders whose natural mucin had been removed. To determine whether sodium pentosanpolysulfate was preventing adherence to the transitional cells by binding the calcium, we treated bladders with sodium pentosanpolysulfate for 30 minutes, rinsed it free, and then instilled the calcium. Adherence of calcium to the bladder epithelium was prevented under these circumstances as well (Table 2).

The concept of bladder-surface glycosaminoglycan as an antiadherence factor active at the cellular, molecular, and ionic levels offers an appealing model of a simple and efficient mechanism by which the bladder might deal with its environment. This mechanism, not limited by the specificity of an antigen-antibody reaction, would enable the bladder to dispose easily of a variety of microorganisms. At the same time, it would prevent calcium, which is often supersaturated in urine, from adhering to the surface and acting as a nidus for stone formation. Furthermore, this mechanism would prevent the adherence of other molecules that could act as a matrix for calcium deposition. It is possible that bladder-surface glycosaminoglycan reduces the interaction of potential carcinogens with the transitional cells.

The urinary tract may not be the only mucous surface in the body to rely on sulfonated glycosaminoglycans as antiadherence factors. The surface of the eye is lined with a heparinlike substance (*10*), and commercial heparin is purified from the gastrointestinal tract of the pig. Endothelial cells of blood vessels also synthesize heparin, which lines the blood vessel walls (*11*, *12*); the advantages of the presence of an antiadherence factor in the vascular system are obvious.

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Olfactory Sensitivity in Humans: Genetic Versus Environmental Control

Abstract. *Olfactory sensitivity to acetic acid, isobutyric acid, and 2-sec-butyl-cyclohexanone was tested in 97 adult male twin pairs to determine the extent to which variation in odor perception was genetically determined. Analysis of the data revealed no evidence for heritability of olfactory sensitivity. However, factors significantly associated with odor perception included cigar, pipe, and cigarette smoking; body fatness; alcohol consumption; and diabetes mellitus.*

Current theories of sensory perception in humans suggest that variation in the ability to detect odors may have a significant genetic component. General sensitivity to odors is thought to be influenced by congenital conditions and by the endocrine status of the body (*1*). Specific sensitivity to an odor may be determined by the functional group, molecular size, or molecular shape of the odorant (*2*, *3*). It has been proposed that perception results from the "fit" of an odorant to receptor sites in the olfactory organ (*2*, *3*). A logical assumption is that variation in the structure of the olfactory receptors may be genetically controlled (*4*). Although observed threshold distributions (*4*, *5*) are compatible with genetic mechanisms, and insensitivity to particular odors (that is, specific anosmias) clusters in families (*6*), little is actually known about heritability over the range of odor sensitivity.

A unique opportunity to investigate genetic variability of olfactory sensitivity arose at the inception of the National Heart, Lung, and Blood Institute (NHLBI) twin study. Participants in this multicenter study were male veteran twins, aged 42 to 56, who were ascertained from the National Academy of Sciences–National Research Council Twin Registry (*7*) and who volunteered to undergo a physical examination at the invitation of the NHLBI (*8*). Tests of olfactory sensitivity were successfully administered to 97 twin pairs, 51 monozygotic (MZ) and 46 dizygotic (DZ), examined at the Framingham, Massachusetts, study center.

Twin populations are ideal for studying the extent to which variation in a characteristic may be genetically determined. Classical twin analysis (*9*, *10*) attempts to relate the similarity between MZ twins, who share all of their genes, to the similarity between DZ twins, who share, on the average, 50 percent of their genes. In this study, evidence for genetic control of odor perception existed if, under certain basic assumptions, olfactory sensitivity was more similar (more highly correlated) for MZ than DZ twin pairs.

An individual's olfactory sensitivity was determined by exposing him to serial dilutions of three chemical compounds thought to represent different "primary" odors as described in Amoore's early stereochemical theories (*3*, pp. 96–125; *5*). The compounds used were acetic acid, isobutyric acid, and 2-*sec*-butyl-cyclohexanone (cyclohexanone), belonging

Table 1. Summary of the twin analysis for olfactory sensitivity. Results are adjusted for examination time. The number of twin pairs is shown in parentheses. Estimates of genetic variance using the method of Christian *et al.* (*10*) were not significant and therefore are not shown.

Chemical compound	Intraclass correlations (r) of sensitivity thresholds*	
	r_{MZ}	r_{DZ}
Acetic acid	0.38 (48)	0.11 (43)
Isobutyric acid	0.23 (47)	0.41 (43)
Cyclohexanone	0.10 (50)	0.04 (44)

*To test the hypothesis that $r_{MZ} = r_{DZ}$, the following normal statistic was used:

$$z = \frac{z_{MZ} - z_{DZ}}{\sqrt{\sigma^2_{MZ} + \sigma^2_{DZ}}}$$

where

$$z_{MZ} = .5\left(\log_e \frac{1 + r_{MZ}}{1 - r_{MZ}}\right)$$

$$z_{DZ} = .5\left(\log_e \frac{1 + r_{DZ}}{1 - r_{DZ}}\right)$$

$$\sigma^2_{MZ} = \frac{1}{N_{MZ} - 3} \quad \sigma^2_{DZ} = \frac{1}{N_{DZ} - 3}$$

and N = number of twin pairs.

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Table 2. Characteristics associated with olfactory sensitivity to isobutyric acid and cyclohexanone. Results are presented in terms of standardized coefficients from stepwise multiple regression analyses adjusted for examination time. The coefficients indicate the relative contributions of the significant independent variables to olfactory sensitivity.

Odor	Regression coefficients					R^2
	Cigar or pipe	Cigarettes	Alcohol	Skinfold thickness	Diabetes mellitus	
Isobutyric acid	.231		−.152	−.227		.11
Cyclohexanone	.208	.189		−.168	.201	.13

to the odor classes of "pungent," "sweaty," and "camphoraceous," respectively. The quality "pungent" may be different from "sweaty" and "camphoraceous" in that it arises, at least in part, from stimulation of the trigeminal nerve and is not strictly an olfactory response (*11*).

Testing each odor required six tubes, each containing 50 ml of solution. The first was filled with distilled water only, and the succeeding five with increasingly stronger solutions of the compound in water. Each participant was instructed to take the first tube (water), unstopper it, hold it within 1 inch of his nose and sniff deeply. The same procedure was followed for each successive tube until the subject indicated that an odor was definitely perceived. The lowest detectable concentration was recorded as the individual's threshold of sensitivity. The compounds were tested in the following order: acetic acid, isobutyric acid, and cyclohexanone.

The three strongest chemical solutions were 25 ml of glacial acetic acid in 975 ml of distilled water, 0.4 ml of isobutyric acid in 1000 ml of distilled water, and a half-saturated solution of cyclohexanone in distilled water. Each of these was diluted by factors of 4, 16, 64, and 256 to obtain the additional chemical strengths. The actual test solutions were kept in stoppered tubes, which were emptied, washed, and refilled frequently to maintain uniform concentrations. It was not possible to conduct the tests in a completely controlled environment with constant temperature, humidity, or purity of background air. However, background exposures should not have affected intratwin-pair or between-zygosity comparisons since both members of a pair were called in for testing on the same day, and MZ and DZ twin pairs were examined randomly throughout the study. In addition, all participants appeared for testing after having fasted.

Since our primary concern was to observe heritability over the range of olfactory sensitivity, formal analysis of the data included only those twin pairs who were able to detect the odor in question. Because odor thresholds decreased as the study continued, all analyses were adjusted for examination time. Although the cause of this decrease could not be ascertained, all analyses, whether adjusted for examination time or not, yielded similar results.

The distributions of odor thresholds for isobutyric acid and cyclohexanone were approximately normal. The distribution for acetic acid deviated from the normal, but only at relatively high concentrations where the acid may behave more like an irritant than an odor.

Results of the twin analyses, shown in terms of the intraclass correlations of sensitivity (Table 1), did not indicate genetic variability of responses. The MZ and DZ twin correlations were not significantly different from one another for any of the odors tested.

The negative findings of the twin analyses suggested that it would be worthwhile to search for other correlates of olfactory sensitivity. Stepwise multiple regression analyses were used to identify characteristics associated with odor threshold for all twins. Variables of interest included age, smoking, drinking and eating habits, respiratory symptoms and disease history, measures of body fatness, and diabetes mellitus. None of these characteristics was significantly associated with olfactory sensitivity to acetic acid. However, cigar or pipe smoking ($P < .01$), skinfold thickness ($P < .01$), and alcohol consumption ($P < .05$) were significantly and independently associated with thresholds for isobutyric acid (Table 2). Individuals who smoked, were lean, or said they drank alcohol infrequently were less sensitive to the odor of this compound than those who were nonsmokers, heavy, or frequent consumers of alcoholic beverages. These three variables accounted for 11 percent (R^2 in Table 2) of the variability in odor threshold. Cigar or pipe smoking ($P < .01$) and skinfold thickness ($P < .05$) were also associated with sensitivity to cyclohexanone. Poor acuity for this odor was related to heavy cigarette smoking ($P < .01$) and diabetes mellitus ($P < .01$) as well. (Of this population, 6 percent were borderline or definite diabetics.) Approximately 13 percent of the total variability in thresholds was explained by the smoking variables, skinfold thickness, and diabetes.

Although the data are sparse and sometimes inconsistent, a few studies have found that smoking and diabetes are related to decreased olfactory sensitivity (*12*). Deterioration of the sense of smell in smokers may be explained by changes in the nasal or olfactory mucosa resulting from exposure to tobacco smoke. Reasons for decreased acuity in diabetics remain more obscure, although cranial neuropathy, not uncommon in diabetics, may account for this finding. The associations of body fatness and alcohol consumption with odor thresholds suggest that heightened olfactory sensitivity may be part of a complex of sensory and psychological responses that includes appreciation of food and drink. This is one aspect of human olfaction that deserves more careful attention.

The results of this study suggest that heredity is not a significant factor in normal perception of these odorants. In fact, twin analyses adjusted for all environmental characteristics associated with sensitivity to each odor supported the original negative results. In addition, analysis of the data including the anosmics, who comprised only 5 percent of the twin population, did not offer an argument for heritability. Not one of the 97 twin pairs was concordant for a specific anosmia. The only characteristic found to be significantly associated with odor blindness was the occupation of firefighter ($P < .001$); all three anosmic firemen were incapable of smelling the same "sweaty" odor of isobutyric acid.

Although the other factors considered here explain only a small proportion of the variability in olfactory sensitivity to isobutyric acid and cyclohexanone, the results indicate that such characteristics may be more influential than heredity in defining the distribution of responses to these odors. In contrast, perception of the odor of acetic acid appears to be unaffected by any of the studied attributes, an observation consistent with the hypothesis that its detection involves a different sensory mechanism.

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Gutless Bivalves

Abstract. *A new benthic species of the protobranch bivalve genus* Solemya, *from the northeastern Pacific Ocean, lacks a gut. It has no internal digestive enzymatic apparatus; nor is there any provision for the secretion of enzymes into the mantle cavity for extraorganismic digestion. The most likely nutritional mechanism for such an animal is the active absorption of dissolved organic molecules from the environment by the large ctenidial lamellae. These are well provided with blood, cleansed of sediment by cilia, and have phosphatases in their epithelial cells.* Solemya borealis *may also be gutless.*

Most bivalve mollusks have a prominent alimentary tract that can easily be discovered by conventional dissection methods. The relatively large stomach is usually surrounded by the digestive diverticula, glandular tissues discernible in the anterodorsal region of the visceral mass without the aid of dissection or microscope. The mouth is often inconspicuous, but the rectum is usually clearly visible next to the posterior adductor muscle. In contrast, members of the protobranch bivalve genus *Solemya* are known for the reduced size of the gut (*1*, *2*). The gut of *Solemya parkinsoni* is so reduced that Owen (*2*) concluded that the species must have some unusual means of augmenting the processes of digestion and assimilation. He proposed that the mantle cavity might act as an organ of extraorganismic digestion.

We have independently of each other discovered a new species of *Solemya* (*3*) and have concluded that this species is gutless. A gross anatomical inspection of the largest specimens available to us, with the aid of a dissecting microscope, revealed no esophageal opening behind the depression representing the mouth, no stomach nor digestive diverticula, and no rectum. Earlier investigators had difficulty tracing the alimentary tracts of other species of this genus because of the gut hypotrophy (*2*, *4*). However, further scrutiny of the new species by means of transverse and longitudinal serial histological sections gave no indication whatsoever of any part of an alimentary system. Specimens of shell length 5 mm to 3 cm were sectioned. The largest of these were sexually mature.

In some animals, glandular tissues from the anterior dorsal region and from within the foot had a superficial resemblance to digestive diverticula; these tissues were tested spectrophotometrically for their ability to digest albumin (*5*). There was no proteolytic activity in the range of hydrogen ion concentrations usually associated with the digestive systems of bivalves (*p*H 5 to 8) (*6*). The tissues in question were later discovered to be spent gonad and pedal gland.

The pedal gland is probably the organ that was suggested as a source of enzymes for extraorganismic digestion in *Solemya parkinsoni* (*2*). This tissue was tested histochemically for esterase and phosphatase activity, α-naphthyl acetate and α-naphthyl phosphate being used as substrates (*7*). A weak alkaline phosphatase activity was found, but the other results were negative. The cells of the pedal gland were strongly stained by Alcian Blue, which indicates the presence of acid mucopolysaccharide. The large pedal gland opens through a pore to the sole of the foot; we conclude that its function is to secrete the large quantities of mucus with which this organism lines its burrows (*8*).

Further to the possibility of pallial digestion, whole animals were fixed briefly in cold, neutral Formalin and incubated in esterase and phosphatase mediums (*7*). A weak phosphatase reaction along the distal edges of the ctenidial lamellae was the only positive reaction over the entire outer surface of the animal. Although we have not exhausted the possibility, we doubt that there is any extraorganismic digestion by endogenous enzymes in the mantle cavity and suggest that the means whereby this species obtains its nutriment is by absorbing dissolved organic molecules. The ctenidia, which are large in comparison with those of most other protobranchs and well supplied with blood sinuses, present a suitable surface area for the absorption of organic molecules (*8*). The presence of phosphatases indicates an active transport mechanism. The foot and mantle may also absorb nutrients.

Symbiotic bacteria in the mantle cavity or in the burrow system could hydrolyze particulate organic material such as wood particles, which are plentiful in the environment. An observation on starch hydrolysis in the mantle cavity of *Solemya parkinsoni* (*2*) hints at the possibility of digestive symbiosis with bacteria. Another source of useful dissolved nutrients could be facultative anaerobic bacteria in the mantle cavity or burrow system (*9*). Stanley (*10*) suggested that bacteria in the burrow of *Solemya velum* might be a source of food.

Although the smallest specimen we sectioned (shell 5 mm long) showed no trace of a gut, the small prodissoconch shell and the size of ova suggest a planktotrophic larva, indicating a functioning gut during early development. The species is benthic and most commonly found burrowing in silt in the vicinity of pulp mills. Whether the pulp mill effluent and wood debris provide food or a congenial environment for symbiotic microorganisms, or whether they simply discourage predators and competitors, remains to be determined.

This new, northeastern Pacific Ocean species of *Solemya* was formerly incorrectly identified with *Solemya panamensis* Dall of the tropical eastern Pacific (*3*). Hypotrophy of the gut is characteristic of the group, but the degree of reduction of the gut cuts across the present taxonomic arrangement, which is based on shell structure. We have examined other species. *Solemya valvulus* Carpenter and *Solemya velum* Say possess small guts similiar to that of *Solemya togata* Poli (*1*). *Solemya panamensis* Dall and *Solemya (=Acharax) agassizii* Dall have vestigial guts similar to *Solemya parkinsoni* Smith (*2*). On the basis of the dissection of a single preserved specimen, *Solemya borealis* Totten appears to be gutless.

The gutless condition of another nonparasitic invertebrate group, the Pogonophora, is well known (*11*). On the basis of their biology, zoologists have been inclined to associate gutlessness with small sessile animals with low energy requirements and large ratios of surface area to

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