than additive. That is, the separate groups tested seemed to be more effective than would have been expected. The basic and acidic amino acids were not significantly effective, whereas all other groups had marked tumor-depressing activity. These results suggested that although there may be some sort of specificity with respect to certain amino acids or types of amino acids, there also appeared to be nonspecificity in that suitable amino acids could satisfy most of an apparently general requirement.

To test the effect of simply raising the nitrogen level of the medium, the addition of ammonium nitrate to the basal medium in concentrations sufficient to double and triple the nitrogen supply showed instead a very slight increase in tumor frequency. To establish that the decrease in tumor frequency produced by the casein hydrolyzate or the amino acid mixture was not simply due to a comparable decrease in general viability, the fully quantitative method was used to determine the viability in each treatment. Although the two additions to the media did depress viability slightly, this was not in proportion to the decrease in tumor counts. The tumor frequencies, when adjusted to percentage viability were: casein hydrolyzate, 57 percent; synthetic "casein hydrolyzate," 47 percent, the basal frequency being expressed as 100 percent. The viability on the casein hydrolyzate was 93.5 percent of that on the basal medium, and on the synthetic "casein hydrolyzate" was 91 percent of the basal value.

It is apparent from these results that it is possible in this system to influence the frequency of occurrence of tumors. Of course, there is no ready way to determine at present whether the potentially tumorous spores do germinate on the amino acid-containing media. They could either not develop at all, or alternatively, they could develop into normal prothalli. The latter case could mean that in the potential tumors there is a block in the pathway from inorganic nitrogen to $-NH_2$ and that the amino acids are in effect satisfying a continuing deficiency, or possibly that the amino acids may be necessary just at the start of physiological activity, perhaps to repair radiation damage (*7*). At present, experiments are being devised to attempt to establish the time relationship of the phenomenon. Since the observation of the amino acid effect, investigations on inorganic nitrogen metabolism have also been initiated. Present results show that with ammonium as the sole source of nitrogen, tumor frequency is highest, whereas with nitrate as the sole source, the frequency is lowest, viability on calcium nitrate being 93.5 percent of that on a nitrogen equivalent of ammonium sulfate. These results would suggest further a possible block in nitrogen reduction from $-NO_3$ to $-NH_4$ associated with the initiation of tumors.

That only a fraction of the total expected number of tumors is affected by any one treatment would suggest that what we recognize as the morphological entity "tumor" actually represents a whole spectrum of biochemical variants. Conceivably, these variants may fall into more general categories in that they affect certain general mechanisms, the dysfunctions of which may also have the general morphogenetic manifestation of tumorization.

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Isolation from Animals of Human Strains of Staphylococci during an Epidemic in a Veterinary School

Abstract. Antibiotic-resistant staphylococci of the same bacteriophage type were isolated from the external nares of asymptomatic domestic animals and from human beings during an epidemic of staphylococcal disease in veterinary students. Not all of the infections could be attributed to person-to-person contact; spread could be explained also by transmission of staphylococci from animals.

An unusual number of senior students at the Veterinary School of the University of Pennsylvania reported to the student health service during the school year 1956–57 with furuncles, cellulitis, deep cutaneous abscesses, and paronychiae. A high incidence of infections continued for the next 2 years, and contact infections in students' families were also observed. Cultures obtained from the lesions and from the external nares of the students yielded hemolytic coagulase-positive *Staphylococcus aureus* of the bacteriophage type 52/42B/81 (type 80/81). The strain was resistant to penicillin, streptomycin, and the tetracyclines and was occasionally resistant to erythromycin; it was sensitive to chloramphenicol and novobiocin.

The external nares of both animals and human beings were swabbed with dry cotton-tipped sticks, which were then rolled on blood-agar plates or, in the third animal survey, on saline (7.5 percent)–mannitol (1 percent) plates, and streaked within 1 hour of swabbing. After incubation overnight, colonies were selected without regard to pigmentation and subjected to the tube-coagulase test with human serum. All coagulase-positive or mannitol-fermenting strains were tested with 23 standard bacteriophages at the routine test dilution (*1*).

In May 1957 questionnaires were distributed to determine the staphylococcal morbidity in the school (Table 1). Thirty-six percent of the seniors reported having had lesions during the school year. The faculty also reported a high incidence (26 percent), but the other three classes of students reported an incidence less than half that of the seniors. Ten of the 11 active lesions cultured yielded staphylococci of strain 80/81.

Nasal swabbing was also performed in May 1957 (Table 1); 46 percent of the seniors carried strain 80/81 staphylococci, whereas the carrier rate in the other five groups was 14 percent or less. Two of the four employees who were carriers were stablemen, and two were office workers. The two faculty carriers and other faculty members who later became carriers all worked in the animal clinics.

During the next school year (1957–58) nasal swabbing of the 46 new seniors was repeated regularly to determine the source of infection. Five seniors were carriers of the 80/81 strain in September 1957; only one of these had been a carrier as a junior. The other four students had worked in the school during the summer. Ten other seniors became carriers before the end of the school year. Lesions developed in all but two of these 15 students. All six of the lesions cultured yielded 80/81 staphylococci. Analysis of the dates on which students were first shown to be carriers revealed that they became carriers shortly after they had been in a work group which included a student with an active lesion.

A second morbidity survey and program of nasal swabbing of the students during the school year 1958–59 (Table 1) showed, as the first had, that the current seniors most frequently gave a history of a recently acquired lesion and most frequently carried the 80/81 strain. In February 1959 no isolation

Table 1. Number of lesions and number of carriers of strain 80/81 staphylococci as determined by nasal swabbing (*5*).

Group	Lesions				Strain 80/81 in nose			
	May 1957		Sept. 1958		May 1957		Feb. 1959	
	*N**	%	*N**	%	*N**	%	*N**	%
Seniors	13/36	36	11/40	28	21/45	46	10/47	21
Juniors	5/42	12	6/39	15	2/46	4	0/34	0
Sophomores	7/40	17	2/47	4	0/45	0	0/52	0
Freshmen	5/46	11	5/53	10	2/51	4	0/41	0
Faculty	5/19	26			2/25	8		
Employees					4/29	14		
Entire group	35/183	19	24/179	13	31/241	13	10/174	6

* Numerator, number yielding positive cultures; denominator, number surveyed or cultured.

Table 2. Isolation of strain 80/81 staphylococci from the external nares of animals in three surveys in 1959.

Animals	No. of cultures*	No. of coagulase-positive isolations†	No. of 80/81 isolations*	Totals for 80/81 isolations	
				N‡	%
Cows	8,8,6	0,1	0,1,0	1/22	4
Horses	10,10,17	0,3	0,1,2	3/37	8
Goats	17,6,8	8,1	3,0,0	3/31	10
Sheep	7,4,0	1,0	0,0	0/11	0
Cats	6,0,0	2	0	0/6	0
Dogs	38,23,42	19,10	6,4,5	15/103	15
Entire group	210	45/137‡	22	22/210	10

* The results of surveys 1, 2, and 3 are given in order. † Results of surveys 1 and 2 only. ‡ Numerator, number of positive isolations; denominator, number of cultures.

of 80/81 staphylococci was made in the other three classes; however, the prevalence of carriers among the seniors was 21 percent.

Because the veterinary students first work regularly in the animal clinics when they are seniors, cultures were obtained from animals in the hospital. Sporadic culturing of lesions in animals resulted in the isolation of typable staphylococci on three occasions (type 80/81 in each case), from lesions of canine dermodectic mange, from a carbuncle in a dog, and from the milk of a cow with mastitis. Random swabbing to detect carriers among 4 cows, 17 horses, 4 sheep, and 7 goats in 1957 did not yield typable strains.

Swabbing of the external nares of animals was repeated three times in 1959 (Table 2). Coagulase-positive staphylococci were isolated from 33 percent (45/137) of the animals cultured in the first two surveys. Type 80/81 staphylococci were isolated from 4 percent of the cows, 8 percent of the horses, 10 percent of the goats, and 15 percent of the dogs in the three surveys. The strain was not isolated from a small number of sheep and cats.

The only other types isolated were type 7 from three dogs, types 7/47/53/54/75/77/VA4 and 7/42E/47/54/73/75 from two other dogs, and type 3B/6/7/42E/54/73/75 from a horse. Only one animal, a dog, had a lesion from which type 80/81 was isolated. There was no evidence of enzootic or epizootic staphylococcal disease in the veterinary hospital during the study.

Two of the animals that carried 80/81 staphylococci had recently entered the hospital; a dog was found to harbor the microorganisms on its third day in the hospital, and a horse, on its first day in the hospital. Findings were positive for other animals on the 13th, 15th, and 26th day in the hospital, respectively. Thus, newly admitted animals as well as long-term residents were shown to be carriers of 80/81 staphylococci.

The isolation of strain 80/81 from asymptomatic animals in association with outbreaks in human beings has not been reported previously, but sporadic isolations of types of staphylococci that infect human beings have been made from animal lesions (*2*). Perhaps the epidemic under discussion was perpetuated by person-to-person spread exclusively. In this event the staphylococci found in the animals may merely reflect general environmental contamination with the organisms, or colonization of the nares without epidemiologic significance. The isolation of 80/81 staphylococci from employees who did not handle animals suggests that person-to-person spread did occur.

On the other hand, the concentration of lesions and carriers in three successive senior classes seems to suggest an additional mode of transmission. The localization of illness in the only class to have close contact with animals and the use of antibiotics in large amounts in the veterinary hospital raised the possibility that the animals were a reservoir for antibiotic-resistant, pathogenic staphylococci that could infect students. A student with a lesion might act as a source of infection for animals, which would then transmit the organism to other students.

Lack of evidence of association with recently hospitalized persons or newborn infants such as is commonly found in outbreaks of staphylococcal disease suggested that this epidemic might represent a major infiltration of "hospital" staphylococci into the community at large. On the other hand, another instance of human staphylococcal disease, apparently due to the 80/81 strain, at a second veterinary school (*3*) suggests that persons in veterinary hospitals may be subject to increased hazard of staphylococcal infection. In this second outbreak, 44 percent of the lesions were reported by seniors; most had occurred 1 to 6 months earlier. No relation between the epidemic among veterinary students and association with human hospital patients was found, nor was this second epidemic related to an epizootic.

These findings have potential experimental significance. Induction of the carrier state in animals would be of value in elucidating their role in the spread of pathogenic staphylococci. This would provide a useful model to study the relation between pathogenic staphylococci and their hosts (*4*).

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