STUDIES ON THE ARIZONA GROUP OF *ENTEROBACTERIACEAE*

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I. DEFINITION OF THE ARIZONA GROUP

The Arizona group of the family *Enterobacteriaceae* is composed of bacteria closely related to the members of the genus *Salmonella* but distinguishable from them by biochemical methods. The biochemical properties of the two groups are delineated in table 1. The reactions listed are those given by typical members of the two groups and exception may be taken to them on the ground that the two reaction patterns are very similar and that not every culture of the groups adheres to the patterns delineated. For instance, a number of well known *Salmonella* types fail to ferment dulcitol and a few rare types liquefy gelatin. Nevertheless, the tests listed above are those used in the laboratory for primary group differentiation of *Enterobacteriaceae* and when interpreted judiciously in combination with the results of serologic examination, an excellent indication can be obtained as to which of the two groups a given culture belongs. Gelatin liquefaction is a very constant property of the Arizona group and the test can be made much more useful if the rapid method of Kohn as modified by Lautrop (27) is used.

Certain additional tests are of value in differentiating the two groups. Schaub (34) noted that Arizona strains utilized malonate whereas salmonellae did not. This observation was confirmed by Shaw (37). Kauffmann and Petersen (25) noted that salmonellae utilized D-tartrate, mucate, and citrate rapidly, whereas Arizona cultures did not. In the examination of a large series of *Salmonella* and Arizona cultures, Ellis *et al.* (17) confirmed all the above-mentioned observations with the exception that 33.2 per cent of 457 monophasic Arizona strains tested utilized mucate within 20 hr, whereas none of 164 diphasic strains did so. Twelve reaction patterns were obtained in testing 1136 salmonellae and 621 Arizona strains in the four organic acid media. Six of these reaction patterns contained 93.7 per cent of the salmonellae whereas three other patterns contained 98.7 per cent of the Arizona cultures. The results are summarized briefly in table 2.

At the time Edwards *et al.* (16) published an extended study of Arizona serotypes, some difficulty was encountered in framing a definition of the group. Subsequently the KCN test as modified by Moeller (29) and the lysine decarboxylase tests of Moeller (30) and of Carlquist (6) have come into general use so that no difficulty now is experienced in distinguishing Arizona strains from those of *Citrobacter* (*Escherichia freundii*) (Edwards and Fife (10); Edwards *et al.* (13)). Certain biochemical characteristics of Arizona strains are somewhat less uniform than those of *Salmonella* serotypes. In studying the ability of the two groups to grow in KCN medium, Edwards and Fife (10) found that whereas only 1.1 per cent of the *Salmonella* strains tested were positive, 7.7 per cent of the Arizona strains were able to initiate growth. It should be stated, however, that the majority of Arizona cultures which were KCN positive belonged to O group 21 and that strains of the O group were almost constantly positive. When cultures of O group 21 were excluded, only 3.3 per cent of the Arizona cultures

[1] Presidential Essay for 1959.

TABLE 1

Major biochemical properties of the genus Salmonella and the Arizona group

Property	*Salmonella*	Arizona
Indole production	−	−
Methyl red test	+	+
Voges-Proskauer test	−	−
Growth in Simmons' citrate	+	+
H_2S production	+	+
Urease production	−	−
Growth in KCN medium	−	−
Motility	+	+
Gelatin liquefaction	−	(+)
Lysine decarboxylation	+	+
Phenylalanine deamination	−	−
Gas from glucose	+	+
Fermentation of:		
Lactose	−	+ or X
Sucrose	−	−
Mannitol	+	+
Dulcitol	+	−
Salicin	−	−
Adonitol	−	−
Inositol	d	−

+ = Prompt, positive, 1 to 2 days; (+) = delayed positive; X = late and irregularly positive; d = different biochemical types; and − = negative.

TABLE 2

Reactions of Salmonella and Arizona cultures in organic acid media

Culture	Mucate	D-Tartrate	Citrate	Malonate
Salmonella	+	+	d	−
Arizona	d	−	−	+

+ = Visible utilization within 20 hr at 37 C; − = no visible utilization within 20 hr at 37 C; and d = different biochemical types.

tested were positive. In the study of 271 Arizona cultures isolated from snakes, LeMinor *et al.* (28) found that 20.8 per cent produced indole and that 3.6 per cent fermented sucrose. However, it should be emphasized that those biochemically aberrant cultures belonged to serotypes recognized with extreme rarity in man and domestic animals so that the percentage of such cultures among the total number of Arizona strains studied was very low.

Through the use of the biochemical tests outlined above, combined with knowledge of the biochemical properties of well known *Salmonella* types, and the serologic results obtained with a given culture, microorganisms may be assigned to the proper group with certainty. Admittedly, cultures exist which present difficulty in placement, but these have amounted to no more than 25 cultures among more than 30,000 cultures of the two groups which have been classified.

II. HISTORY OF THE ARIZONA GROUP

The first description of an organism now classified in the Arizona group was that of Caldwell and Ryerson (5) in which attention was called to a bacterium isolated from diseased chuckwallas (*Sauromalus ater*), horned lizards (*Phrynosoma solare*), and Gila monsters (*Heloderma suspectum*). This organism was designated *Salmonella* sp. (Dar-es-Salaam type, var. from Arizona) because it liquefied gelatin as does the true Dar-es-Salaam type although it possessed little antigenic relationship to the latter. Although lactose fermentation was not observed, an acid coagulation of milk by the reptilian strains was recorded. Kauffmann (24) later studied a culture of this type and although he recognized that it fermented lactose and liquefied gelatin, placed it in the genus *Salmonella* because of the close relationship of its H antigens to those of known *Salmonella* types. The organism was called *Salmonella arizona* and assigned the antigenic formula 33: z_4, z_{23}, z_{26} by Kauffmann.

Peluffo *et al.* (32) studied seven related cultures, including the original Arizona strain, and noted that all fermented lactose and liquefied gelatin. The bacteria were biochemically similar and all were serologically related. It was concluded that the cultures were *Enterobacteriaceae*, the biochemical properties of which differed from those of any of the genera then recognized. Edwards *et al.* (12) described 44 cultures isolated from reptiles, fowls, mammals, and man, and found that they were divisible into 15 epidemiologically significant serologic types. The cultures possessed similar biochemical properties and, directly or indirectly, were related serologically to the original Arizona strain. Some of the cultures had H antigens which were unrelated to

those of the Arizona strain. However, such strains had O antigens identical with cultures which did possess flagellar relationships to that organism. Thus, it became apparent that there existed a group made up of a discontinuous series of related types much broader in its antigenic constitution than had previously been recognized—the Arizona group. The cultures were derived largely from pathological processes, and identical serotypes were demonstrated to be epidemiologically related.

Edwards and West (11) described a bacterium isolated from a snake which fermented lactose promptly and which displayed the typical phase variation of Andrewes (1). The organism possessed biochemical characteristics similar to those of the Arizona group which previously was made up entirely of monophasic cultures. West *et al.* (39) described eight additional diphasic cultures which together with the above-mentioned strain, were assigned to the Arizona group. Thus, it became apparent that the Arizona group, like the closely related salmonellae, was made up of both monophasic and diphasic types which, almost without exception, possessed O and H antigens related to those of known *Salmonella* types.

The first comprehensive study of the biochemical and serologic properties of the Arizona group was published by Edwards *et al.* (16) who studied 382 cultures derived largely from fowls, spray-dried egg powder, and reptiles. These were divisible into 25 O groups and 61 serologic types. Although a large number of serotypes subsequently were described in a long series of papers with various collaborators, no comprehensive review of the serologic properties and relationships of the Arizona group since has been published. Many new antigens were recognized and many undescribed relationships detected in the intervening years and therefore a summary of the serology of the group as it now is known is included.

Since the Arizona group was first established, reports have appeared which emphasize its importance in diseases of animals and man. Gopher snakes captured on farms where Arizona infections occurred among turkeys were found to be carriers of the serotype found in the poults (Hinshaw and McNeil (21)). Later the same authors (22) isolated Arizona serotype 7: 1, 7, 8 (numbers to the left of the colon denote O antigens; numbers to the right, H antigens) from a number of outbreaks in poults and showed that all the infections were traceable to eggs produced in a restricted area in California. Feeding experiments with poults and chicks lent support to the conclusion that serotype 7: 1, 7, 8 was responsible for the disease. Hinshaw and McNeil (23) also reported the isolation of serotype 7: 1, 7, 8 from a number of rattlesnakes kept in a single pen and the autopsy findings indicated that this serotype was responsible for the death of the snakes.

In the studies of Edwards *et al.* (16) it was demonstrated that epidemiological data could be correlated with serologic properties and, that, in turkeys, the infections were spread through the medium of eggs. Transmission of given serologic types from hatchery to hatchery and from state to state could be traced with accuracy. The organisms were associated with severe infections of young fowls in which the mortality was high. Experiments in which normal chicks were exposed to artificially infected birds demonstrated that the bacteria were capable of initiating fatal infections in fowls. The bacilli also were thought to be pathogenic for reptiles, since they were repeatedly recovered from the internal organs of snakes under conditions which indicated that they were responsible for fatal infections. Only 4 of the 382 cultures studied were isolated from man, 3 from the stools of persons affected with gastroenteritis, and 1 from an hepatic abscess at autopsy. The cultures of human origin were so few in number that it was impossible at that time to judge the role of the bacteria in enteric infections of man.

Bruner and Peckham (2) isolated the same serotype as that studied by Hinshaw and McNeil (22) from an infection of poults at a Pennsylvania hatchery which obtained eggs from California. Goetz *et al.* (20), in an illuminating study, conducted agglutination tests on turkeys in flocks known to harbor serotype 7: 1, 7, 8. Reactors were found and eggs from these birds were incubated. Both the eggs and embryos were found to contain the Arizona serotype 7: 1, 7, 8. Ryff and Browne (33) isolated a diphasic Arizona type (26: 29-30) from the fetuses in an outbreak of abortion in ewes.

Reports on the presence of the Arizona group in infections of man have also accumulated in the literature. Seligmann *et al.* (36) recorded the isolation of a culture identical with the original

Arizona strain from the feces of a woman affected with fever, vomiting, and diarrhea. Edwards (7) reported the isolation of an Arizona strain belonging to serotype 10: 1, 2, 5 from the feces of an 11-month-old baby affected with acute colitis.

Ferris *et al.* (18), in Australia, isolated a salmonella-like organism from 26 out of 29 cases of a disease characterized by vomiting, diarrhea, and fever. The infection occurred among the personnel of a single hospital. Although the bacteria were never identified as to serotype, the description of their biochemical and serologic properties leaves no doubt that they were Arizona strains. So far as is known this is the first recorded occurrence of the organisms in a mass infection in man. However, shortly afterwards Verder, Bell, Collins, Schreiber and Brennan (*unpublished data* quoted by Murphy and Morris (31)) studied an outbreak of 51 cases of gastroenteritis which occurred among a group of 158 student nurses in a hospital in Washington, D. C. An organism identified by Edwards and West (*unpublished data*) as Arizona serotype 1, 2: 1, 2, 5 (*i.e.*, an organism identical with the original Arizona type) was recovered from 70 per cent of the patients but from none of 16 unaffected persons of the group. Many of the cases were severe and required hospitalization for some days. Rises in the agglutinin titer for the Arizona culture were observed.

Buttiaux and Kesteloot (4), in France, isolated Arizona strains from the feces of six persons; three were affected with an acute dysentery-like syndrome, one with enteric fever, and two with chronic colitis. One of the cultures was identical with the original Arizona type, one contained O antigen 7, and three contained O antigen 12. The authors drew attention to the likelihood that the infections were contracted from contaminated eggs or egg powder. Murphy and Morris (31) described two well defined outbreaks of infection in man. The first occurred among six children from three families who had eaten a common lunch. Ice cream was thought to be the vehicle of infection. The children were acutely ill with fever, vomiting, and diarrhea. All of the children developed O agglutinins for serotype 10: 1, 2, 5 which was isolated from the stools of all. The second episode, which also involved serotype 10: 1, 2, 5 occurred among six patients in a hospital ward for whom a special beverage had been prepared by an employee who was just recovering from diarrhea of 3 days' duration. The organism was recovered from the stools of three of the six persons affected with fever, vomiting, diarrhea, and prostration and from the feces of the employee who had prepared the food.

Seligmann and Saphra (35) reported the isolation of serotype 5: 1, 2, 10 from the blood and the feces of an 8-month-old baby affected with a prolonged illness, characterized by fever, diarrhea, and malaise. Butt and Morris (3) isolated serotype 5: 13, 14 from the pus in a case of otitis media. The patient ran a prolonged continuous fever and was hospitalized for more than a month. The blood and stool cultures were negative, but the serum of the patient contained O (1-320) and H (1-5120) agglutinins for the Arizona strain.

Edwards *et al.* (14, 15) reported 1308 cultures of the Arizona group, of which 87 were isolated from man. Attention was called to the occurrence of these organisms in severe outbreaks of infection in animals and in severe diarrhea and gastroenteritis in man as well as to their marked tendency to invade the blood and to produce localized infections in man. Details concerning the clinical conditions from which the strains of human origin were isolated were included in these publications. Krag and Shean (26) described two fatal infections which were attributed to type 7: 1, 2, 6. In one case a liver abscess was observed, whereas arthritis and osteomyelitis occurred in the second. The bacilli were isolated from the lesions and in one case agglutinins for the Arizona serotype were demonstrated.

III. SEROLOGIC DIFFERENTIATION OF ARIZONA TYPES

The methods used in the differentiation of serotypes were those detailed by Edwards and Bruner (8) and Edwards and Ewing (9) and will not be described. The cultures upon which the work was based were received over a period of 20 years and were isolated largely in the United States. However, a significant proportion of the cultures, particularly those isolated from reptiles, were isolated in other countries. The reptilian cultures were isolated in many different countries and included strains from South America, Europe, Africa, and Asia.

Thirty-two O groups were recognized, of which three (O7, O9, and O10) each was divided into two subgroups. Some degree of cross reaction among the O groups was noted and the reactions of the individual antigens with the various sera are included in table 3. Obviously, some of the sera agglutinated heterologous antigens to such

TABLE 3

Reactions of unabsorbed Arizona O sera

Arizona O Antigen	Homologous Titer	Titers with Heterologous Sera
1, 2	5120	*1,3*-320; *1,33*-20; *9a,9b*-320
1, 3	2560	*1,2*-5,120;*1,4*-40; *7a,7b*-160; *9a, 9b*-160; *12*-80; *17*-160;*27*-20; *28*-160; *1,33*-20
1, 4	2560	*12*-40; *17*-40
1, 33	5120	*1,2*-640; *1,3*-20; *7a,7b*-20; *9a, 9b*-20; *12*-20; *14*-20; *16*-20; *25*-40; *26*-20
5	5120	*26*-20; *29*-640
6	5120	*7a,7b*-20; *7a,7c*-80; *8*-20
7a, 7b	2560	*7a,7c*-640; *8*-40; *25*-20; *27*-40; *32*-40
7a, 7c	2560	*7a,7b*-160; *8*-80; *27*-20; *32*-40
8	1280	
9a, 9b	2560	*9a,9c*-10,240; *18*-20
9a, 9c	5120	*9a,9b*-640; *18*-20
10a, 10b	1280	*1,2*-80; *10a,10c*-320; *24*-20
10a, 10c	640	*6*-40; *10a,10b*-40; *14*-20
11	1280	*9a,9c*-40
12	2560	*1,4*-40; *28*-40; *30*-20
13	1280	*9a,9b*-80; *17*-320; *18*-20; *27*-320; *28*-40; *30*-40
14	1280	*1,2*-40; *5*-320; *10a,10c*-20; *17*-20; *30*-20; *32*-20
15	2560	*1,2*-20; *9a,9b*-160; *9a,9c*-20; *17*-40; *28*-20
16	1280	*1,2*-160; *22*-20
17	5120	*1,4*-160; *10a,10c*-40; *12*-80; *25*-20; *28*-80
18	2560	*9a,9c*-160; *21*-40
19	1280	*5*-80; *18*-20; *28*-20
20	1280	*9a,9c*-160; *10a,10c*-20
21	1280	*8*-20; *10a,10c*-20; *18*-40
22	2560	*10a,10c*-160; *31*-20
23	1280	*1,2*-160; *1,3*-40; *28*-160
24	1280	*8*-40
25	2560	*8*-20; *17*-20
26	2560	*5*-40; *9a,9c*-40; *27*-40; *30*-160
27	2560	*7a,7b*-80; *7a,7c*-80; *17*-20; *24*-40
28	640	*5*-160; *23*-20; *29*-320
29	640	*5*-160
30	2560	*5*-20; *8*-40; *15*-20; *23*-80; *25*-160; *28*-40; *31*-40
31	640	
32	2560	*1,4*-20; *7a,7c*-320; *10a,10c*-320; *24*-160; *31*-20

Antigenic symbols italicized.

an extent that absorption was necessary to produce sera which could be used in simple slide agglutination tests for group and subgroup determination. The absorptions necessary to produce such sera are listed in table 4. Sera so absorbed contained strong specific fractions and were used in slide agglutination tests for O group determinations without difficulty. The majority of the O antigens listed in table 3 possessed strong reciprocal relationships to, or were identical with, one of the known *Salmonella* O antigens. These relationships are listed in table 5. Undoubtedly, additional minor relationships exist between the O antigens of the two groups but those included in the table represent the strong, reciprocal relationships noted by the writers.

The H antigens of Arizona strains possessed

TABLE 4

Absorption of sera for specific O factors

O Factor	Serum Strain		O Antigens Used in Absorptions
	No.	Formula	
2	DC 5	1, 2: 1, 2, 5	1, 3 + 1, 33
3	699-52	1, 3: 1, 2, 5	1, 2
4	292-53	1, 4: 1, 2, 5	1, 2 + 1, 3
5	1840-54	5: 17, 20	14 + 29
6	So50	6: 13, 14	Unabsorbed
7b	2432-53	7a, 7b: 1, 2, 6	7a, 7c
7c	143-57	7a, 7c: 27-31	7a, 7b + 32
8	CDAI 426	8: 1, 7, 8	Unabsorbed
9b	N 99	9a, 9b: 13, 15	9a, 9c
9c	3600-56	9a, 9c: 33-31	9a, 9b + 18 + 20
10b	3970-53	10a, 10b: 1, 2, 5	10a, 10c
10c	396-56	10a, 10c: 13, 15	10a, 10b + 32
11	Ore 181	11: 16, 17, 18	Unabsorbed
12	124-57	12: 27-28	Unabsorbed
13	1715-50	13: 1, 2, 5	Unabsorbed
14	Pc 123	14: 1, 6, 7, 9	Unabsorbed
15	5320-52	15: 1, 2, 6	Unabsorbed
16	So 34	16: 13, 14	Unabsorbed
17	M 98	17: 29-25	1, 3 + 13
18	So 5	18: 13, 14	Unabsorbed
19	Pc 145	19: 1, 2, 5	Unabsorbed
20	Pc 148	20: 1, 2, 6	Unabsorbed
21	1450-53	21: 1, 2, 6	Unabsorbed
22	2959-55	22: 1, 2, 5, 6	Unabsorbed
23	5395-52	23: 33-25	Unabsorbed
24	Pc 196	24: 26-25	32
25	Pc 110	25: 27-28	30
26	4859-52	26: 23-30	Unabsorbed
27	PM 11	27: 23-25	13 + 32
28	3592-56	28: 23-25	1, 3
29	557-52	29: 33-31	5 + 28
30	4602-54	30: 23-31	26
31	3853-54	31: 23-25	Unabsorbed
32	1675-55	32: 1, 2, 6	24
33	255-58	1, 33: 23-21	1, 2 + 1, 3

TABLE 5

Relationships between the O antigens of Salmonella spp. and the Arizona group

Arizona O Antigen	Related *Salmonella* Antigen
1, 2	*51*
1, 3	*44*
5	48
7a, 7b	*18*
9a, 9c	*50*
10a, 10b	40
10a, 10c	49
11	45
12	17
13	*41*
15	*42*
16	*38*
17	*11*
18	1, 13, 23
20	*35*
21	43
22	21
23	47_1, 47_2 (*S. bergen*)
25	16
27	6, 7
28	47_1, 47_3 (*S. kaolack*)
31	*52*
32	*6, 14, 24*

Italics indicate antigenic identity.

many strong intragroup relationships as well as relationships to a number of *Salmonella* H antigens. The H antigens recognized, together with their cross reactions with other antigens, are listed in table 6. Many of the relationships were represented by the use of common symbols. In other instances, relationships equally as strong were not so denoted. This situation was the result of undetected unilateral relationships, to lack of a cross-reacting agglutinin in the first lot of antiserum prepared for a newly delineated antigen, or to incomplete suppression of one phase when a diphasic culture was used for immunization. The absorptions necessary to produce specific H sera for use in diagnosis are listed in table 7.

In tables 4 and 7, many of the sera were absorbed to produce single factors. In some instances the need for absorption was not reflected in the reactions listed in tables 3 and 6. All lots of serum produced from a given culture did not exhibit the same degrees of cross reactivity and many of the absorptions listed in the table

TABLE 6

Reactions of unabsorbed Arizona H sera

Arizona H Antigens	Homologous Titer	Titers with Heterologous Arizona Sera
1, 2, 5	12,800	*1,2,5,6*-12,800; *1,2,6*-3,200; *1,2, 10*-1,600; *1,2,36*-12,800; *1,3,11*-1,600; *1,6,7*-1,600; *1,6,7,9*-1,600; *1,7,8*-200
1, 2, 5, 6	25,600	*1,2,5*-12,800; *1,2,6*-3,200; *1,2,10*-1,600; *1,2,36*-12,800; *1,3,11*-1,600; *1,6,7*-800; *1,6,7,9*-1,600; *1,7,8*-400; *17,20*-200
1, 2, 6	12,800	*1,2,5*-3,200; *1,2,5,6*-6,400; *1,2,10*-6,400; *1,2,36*-25,600; *1,3,11*-1,600; *1,6,7*-25,600; *1,6,7,9*-6,400; *1,7,8*-400
1, 2, 10	25,600	*1,2,5*-400; *1,2,5,6*-200; *1,2,6*-1,600; *1,2,36*-12,800; *1,3,11*-3,200; *1,6,*-7-6,400; *1,6,7,9*-3,200; *1,7,8*-800
1, 2, 36	25,600	*1,2,5,*-25,600; *1,2,5,6*-1,600; *1,2,6*-3,200; *1,2,10*-12,800; *1,3,11*-1,600; *1,6,7*-1,600; *1,6,7,9*-3,200; *1,7,8*-200; *17,20*-200
1, 3, 11	12,800	*1,2,5*-400; *1,2,6*-800; *1,2,10*-6,400; *1,2,36*-6,400; *1,6,7*-400; *1,6,7,9*-800; *1,7,8*-400
1, 6, 7	25,600	*1,2,5*-200; *1,2,6*-6,400; *1,2,10*-6,400; *1,2,36*-1,600; *1,3,11*-1,600; *1,6,*-7,9-6,400; *1,7,8*-1,600
1, 6, 7, 9	6,400	*1,2,5*-800; *1,2,5,6*-200; *1,2,6*-3,200; *1,2,10*-3,200; *1,2,36*-3,200; *1,3,11*-800; *1,6,7*-25,600; *1,7,8*-800
1, 7, 8	6,400	*1,2,5*-800; *1,2,6*-6,400; *1,2,10*-6,400; *1,2,36*-3,200; *1,3,11*-3,200; *1,6,7*-12,800; *1,6,7,9*-6,400
13, 14	25,600	*13,15*-25,600
13, 15	25,600	*13,14*-3,200
16, 17, 18	25,600	*17,20*-3,200
17, 20	25,600	*1,2,36*-400; *16,17,18*-400; *35*-200
21	6,400	*35*-1,600
22	25,600	*29*-6,400; *30*-800; *37*-200
23	25,600	*21*-200; *29*-1,600; *31*-200; *34*-3,200
24	25,600	*25*-400; *33*-800
25	6,400	*31*-200; *35*-800
26	12,800	*23*-1,600
27	25,600	*28*-1,600; *35*-800; *37*-1,600
28	25,600	*31*-200

TABLE 6.—*Continued*

Arizona H Antigens	Homologous Titer	Titers with Heterologous Arizona Sera
29	25,600	*22*-400; *28*-200; *31*-400
30	25,600	*21*-400; *23*-12,800; *29*-800; *34*-1,600
31	25,600	*22*-400; *32*-6,400
32	25,600	*27*-100; *28*-200; *31*-100
33	25,600	*40*-400
34	12,800	*38*-100
35	25,600	*25*-100; *27*-200
37	3,200	*17,20*-100; *31*-200; *35*-100; *38*-200; *40*-400
38	25,600	*40*-800
39	25,600	
40	25,600	*37*-200; *38*-1,600

Antigenic symbols italicized.

No reactions at dilutions less than 1:100 included.

were based on experience with sera of lots other than those illustrated. In actual practice it often was not necessary to use such an array of absorbed sera and the suggested factor sera were poised on the side of safety.

In some instances *Salmonella* sera were used as a source of factor sera or *Salmonella* cultures were used to absorb Arizona sera to produce single factors. This is a reflection of the early work on the group when it was necessary to compare carefully closely related *Salmonella* and Arizona types. The absence of certain H factors, *e.g.*, 4 and 12, is due to their assignment to specific factors present in *Salmonella* cultures that contained antigens z_4, z_{23} and z_4, z_{24}, respectively. It was felt necessary to include these to make more certain the differentiation of cultures of the two groups. Since this system of antigen determination was most satisfactory, its use was continued. The relationships of Arizona H antigens to known *Salmonella* H antigens are listed in table 8. Although the relationships listed in table 8 were strong ones which were apparent in diagnostic work, no instances of complete antigenic identity were noted.

Through the various combinations of O and H antigens observed, an antigenic schema was established. Among 2634 cultures, 180 antigenic combinations or serotypes were recognized. These, together with the number of cultures of each type found and the sources from which they were isolated are given in table 9. Duplicate cultures from the same animal or the same person were excluded from the table. In interpreting the antigenic formulas it should be kept in mind that the numbers appearing to the left of the colon in the formulas denote O (heat stable, somatic) antigens. Thus, an organism designated as 1, 2: 1, 2, 5 belongs to O group 1, 2, whereas an organism possessing the formula 5: 1, 2, 5 is a member of O group 5. O groups 1, 2: 1, 3; and 1, 4 are related serologically and therefore a common symbol is used in the formulas. The symbols to the right of the colon represent the H (flagellar) antigens of the bacteria. There are many complex relationships among the H antigens, and the symbols used by no means indicate all of them. Only those antigens which are important in distinguishing serotypes are expressed. Here again relationship is expressed by the use of common symbols. For instance, types 5: 1, 2, 5; 5: 1, 2, 10; and 5: 1, 3, 11 possess identical O antigens and related but distinct H antigens. Types 5: 13, 14 and 5: 13, 15 possess the same O antigens as the foregoing types but display H antigens which are related to each other but are not related to those of the foregoing types. Further, as in the genus *Salmonella*, both monophasic and diphasic forms occur. The H antigens of the monophasic types are expressed by such symbols as 1, 2, 5 or 1, 6, 7, 9, whereas the diphasic types are indicated by such symbols as 23-21 or 24-28. In the latter H formulas 23 and 24 represent phase 1 antigens, whereas 21 and 28 represent antigens of phase 2. Attention should be called to the organisms listed in the schema as 5, 29: 33-21-40. This was a complex type determined by Edwards, Fife, and LeMinor (*unpublished data*) which had an unusual combination of O antigens as well as three distinct and readily reversible flagellar phases. The occurrence of three naturally occurring, reversible H phases in a single serotype is a hitherto unrecognized phenomenon.

In addition to the total number of cultures of each type recognized, the number of outbreaks or foci of infection is listed in table 9. In most instances the number of cultures is greater than the number of outbreaks, since cultures often were obtained from several persons or animals in a single outbreak of disease. Further, cultures were derived from asymptomatic persons or animals, in which case the cultures were recorded but no outbreak was set forth. In some instances

TABLE 7

Absorption of sera for specific Arizona H factors

H Factor	Serum Strain		H Antigens Used in Absorptions
	No.	Formula	
2...	DC 5	1, 2: 1, 2, 5	*S. duesseldorf* (6, 8: z_4, z_{24})
3...	*S. duesseldorf*	6, 8: z_4, z_{24}	1, 2, 5
5	DC 5	1, 2: 1, 2, 5	*S. cerro* (18: z_4, z_{23}) + 1, 2, 6
6	So 9	9: 1, 2, 6	*S. cerro* (18: z_4, z_{23}) + 1, 7, 8
7...	CDAI 184	7: 1, 7, 8	*S. cerro* (18: z_4, z_{23})
8	CDAI 184	7: 1, 7, 8	1, 6, 7
9	Pc 143	1, 3: 1, 6, 7, 9	1, 2, 6 + 1, 6, 7
10	N 178	1, 3: 1, 2, 10	*S. cerro* (18: z_4, z_{23}) + 1, 3, 11
11	S 39	5: 1, 3, 11	*S. duesseldorf* (6, 8: z_4, z_{24})
13...	NJ 4	13: 13, 14	unabsorbed
14	NJ 4	13: 13, 14	13, 15
15	N 99	9: 13, 15	13, 14
16...	*S. tennessee*	Sa. 6, 7: z_{29}	Unabsorbed
17	Pc 107	5: 17, 20	*S. tennessee* (6, 7: z_{29})
18	Ore. 181	11: 16, 17, 18	*S. tennessee* + 17, 20
20	Pc 107	5: 17, 20	16, 17, 18
21	Pc 195	12: 23-21	35
22	1141	27: 22-31	29 + 31
23	3209-54	28: 23-28	26 + 30
24	Pc 217	24: 24-28	Unabsorbed
25	Pc 155	23: 24-25	24
26	3829-53	9: 26-21	Unabsorbed
27	Pc 110	25: 27-28	Unabsorbed
28	Pc 110	25: 27-28	27
29	16019	26: 29	22 + 30
30	456-53	10: 33-30	22 + 23
31	1106-55	16: 27-31	23 + 29
32	1971-51	28: 32-28	28 + 31
33	466-52	1, 4: 33-31	24
34	599-54	16: 23-34	23 + 30
35	142-56	11: 35-28	21 + 25 + 27
36	1189-56	17: 1, 2, 36	1, 2, 5 + 1, 2, 10 + 1, 3, 11
37	2224-56	16: 22-37	40
38	1995-57	7: 27-38	27 + 40
39	1158-58	16: 39-25	Unabsorbed
40	2907-58	29: 33-40	33 + 37 + 38

it was difficult to decide whether an outbreak should be recorded because it was not always clear whether the Arizona culture isolated from a given source was responsible for the clinical or pathological condition observed. In practically all instances the opinion of the person who isolated the culture or that of the physician or veterinarian concerned was accepted. When insufficient evidence was available upon which to base a logical opinion, no outbreak or focus of infection was recorded.

IV. OCCURRENCE AND DISTRIBUTION OF THE ARIZONA GROUP

The cultures isolated from fowls and reptiles composed almost 75 per cent of the cultures studied. The preponderance of cultures from these sources was accounted for by several facts. The cultures from reptiles included many isolated during the course of extensive surveys. Arizona types long have been known to be prevalent in turkeys in this country. Twenty years ago when the organisms first were recognized in infections of turkeys, poults from each hatchery harbored

TABLE 8

Relationships between the H antigens of Salmonella spp. and the Arizona group

Arizona H Antigen	Related *Salmonella* H Antigen
1	z_4
2	z_{23}
3	z_{24}
5	z_{26}
10	z_{22}
13	g...
16	z_{29}
20	z_{36}
21	z_{35}
22	k
23	l, z_{13}
24	r
27	z_{10}
28	e, n
29	k
30	1, 5
31	z
32	c
33	i
35	a

a single serotype and through examination of cultures isolated from infected poults it could be determined with accuracy from which hatchery they originated. This situation probably was due to the sporadic occurrence of the organisms in individual turkey flocks and the rapid dissemination of the organisms when the eggs from infected flocks first were collected with those from other flocks in large hatcheries. The individuality of types associated with given hatcheries no longer exists to its previous extent since there has been an extensive interchange of eggs and supply flocks among the establishments.

The number of cultures derived from chickens was relatively small and this is surprising when the relative numbers of chickens and turkeys in the animal population are considered. However, it must be remembered that the individual turkey is more valuable than a single chicken and hence more likely to be presented for postmortem examination. Among cultures of all categories received for diagnosis, those isolated from turkeys greatly outnumbered the cultures from chickens. The seeming disparity of incidence of the organisms in the two species probably is more apparent than real. Solowey (38) found many Arizona strains in egg powder and this indicates that the organisms are present in chickens. Many serotypes have been found in egg powder which have not been recognized in fowls, indicating that chickens have not been examined to a sufficient extent to determine the true incidence of the organisms.

The original strains of the Arizona group were isolated from reptiles and organisms belonging to the group continued to appear among cultures from reptilian sources. The cultures listed were isolated largely from snakes but a small proportion were found in various species of lizards and tortoises. Outbreaks of infection in reptiles were recorded simply because the persons who isolated the cultures attributed etiologic importance to the isolated cultures. Recently, LeMinor *et al.* (28) reported the presence of Arizona types in 44.8 per cent of 310 apparently normal snakes examined. The reptiles were captured in France for collection of venom and were not associated in captivity. Salmonellae were found only in 1.8 per cent of these reptiles. If these figures represent the incidence of Arizona types in reptiles in other areas, the assignment to the organisms of any etiologic role in reptilian infections would seem unwarranted. Therefore, the instances in which infections in reptiles were attributed to the organisms must be discounted.

The sources of the cultures isolated from animals other than turkeys, chickens, reptiles, and man are listed in table 10. The organisms occurred both in normal and diseased animals. In some instances the organisms seemed to be responsible for severe infections. Type 13: 13, 14 was the only etiologic agent recognized in two highly mortal outbreaks of disease in canaries. Type 26: 23-30 appeared repeatedly in monkeys affected with diarrhea in which no shigellae or salmonellae were found. This type appeared in monkeys in the United States, Canada, and Europe. It would appear, therefore, that the animals were infected in collecting pens before shipment from the country of origin. This probably explains the widespread and frequent occurrence of this type in monkeys. The close association of type 26: 29-30 with sheep was notable. Aside from one culture isolated from a turkey, the organism appeared only in sheep and was found in New York, Minnesota, Nebraska, North Dakota, Wyoming, California, France, and Germany. Whether this close association of a serotype to an animal species represents a host

TABLE 9

Distribution of Arizona serotypes according to source

Serotype	Turkeys		Chickens		Reptiles		Man		Other Animals		Other Sources		Total	
	Outbreaks	Cultures	Outbreaks	Cultures	Outbreaks	Cultures	Outbreaks	Cultures	Outbreaks	Cultures	Eggs and egg products	Water, sewage, misc.	Outbreaks	Cultures
1, 2: 1, 2, 5			1	1	2	2	4	10		1	6		7	20
1, 3, 11	2	3									2		2	5
26-31						1								1
33-21						1								1
1, 3: 1, 2, 5	17	18			1	1			1	1		1	19	21
1, 2, 6					1	3					1		1	4
1, 2, 10							2	2					2	2
1, 3, 11					2	3			1	2			3	5
1, 6, 7, 9	3	3			1	1							4	4
1, 7, 8										1				1
1, 4: 1, 2, 5	47	90	1	1	3	10	4	4	2	2	2	1	57	110
1, 2, 6					1	1	1	1					2	2
1, 3, 11							1	1					1	1
13, 14											1			1
26-25						1								1
28-38						2								2
29-28						2								2
33-31										1				1
1, 33: 23-21						1								1
24-25						1								1
26-31						1								1
5: 1, 2, 5					1	1	1	3			3	4	2	11
1, 2, 10							1	1					1	1
1, 3, 11	1	1					1	1			3		2	5
1, 7, 8	1	1											1	1
13, 14	18	43	6	8			6	7	3	4	10		33	72
16, 17, 18											1			1
17, 20	34	53	1	1	1	2	1	3		1	1		37	61
24-28						2								2
26-31						1								1
29-30						2								2
6: 1, 2, 5	1	1											1	1
13, 14											4			4
7: 1, 2, 5											2			2
1, 2, 6	289	364	6	6	2	4	86	98			1		383	473
1, 7, 8	387	773	8	11	1	7	4	19	8	14	2		408	826
27-28						1								1
27-31					2	9							2	9
27-38						1								1
29-25						1								1

TABLE 9.—*Continued*

Serotype	Turkeys		Chickens		Reptiles		Man		Other Animals		Other Sources		Total	
	Outbreaks	Cultures	Outbreaks	Cultures	Outbreaks	Cultures	Outbreaks	Cultures	Outbreaks	Cultures	Eggs and egg products	Water, sewage, misc.	Outbreaks	Cultures
8: 1, 7, 8	1	4			1	1					2		2	7
13, 14											2			2
17, 20											1			1
9: 1, 2, 5	3	3				5				1	9		3	18
1, 2, 6							1	1			1		1	2
1, 2, 10							1	1					1	1
1, 7, 8											1			1
1, 3, 11										1				1
13, 14											7			7
13, 15							2	3					2	3
16, 17, 18											1			1
17, 20			1	2					1	1			2	3
22-31						2								2
23-21						1						1		2
24-31					1	2	1	1					2	3
26-21					1	2							1	2
29-30						1								1
29-31						2								2
33-21						1								1
33-31						24								24
10: 1, 2, 5	2	2	52	89	1	2	17	30	1	17	5	47	73	192
1, 2, 5, 6						2								2
1, 2, 6	1	1			3	3			1	1			5	5
1, 2, 10					1	1	2	2					3	3
1, 3, 11						1		1			7	1		10
13, 14			1	2							19	1	1	22
17, 20			1	1							7		1	8
33-30						2								2
11: 1, 2, 5						1								1
13, 14											2			2
16, 17, 18			1	1					1	1	3		2	5
12: 1, 2, 5												1		1
1, 2, 6			1	1									1	1
1, 6, 7			2	2							1		2	3
1, 6, 7, 9											1			1
1, 7, 8											1			1
17, 20			1	1							1		1	2
23-21											1			1
27-28						43								43
13: 1, 2, 5	1	2			3	7	1	1	1	2	5		6	17
1, 3, 11					1	7							1	7
1, 7, 8											1			1
13, 14									2	4			2	4
13, 15							1	1					1	1
16, 17, 18			1	2							1		1	3
17, 20											2			2

TABLE 9.—*Continued*

Serotype	Turkeys		Chickens		Reptiles		Man		Other Animals		Other Sources		Total	
	Outbreaks	Cultures	Outbreaks	Cultures	Outbreaks	Cultures	Outbreaks	Cultures	Outbreaks	Cultures	Eggs and egg products	Water, sewage, misc.	Outbreaks	Cultures
14: 1, 2, 5									1	1	1		1	2
1, 2, 6							1	1					1	1
1, 6, 7, 9					1	2							1	2
15: 1, 2, 6					1	1							1	1
1, 3, 11	12	31											12	31
13, 14						1						4		5
24-25							1	1					1	1
27-28						1								1
27-31						1								1
16: 1, 2, 7					1	1							1	1
13, 14											3			3
22-21	1	1			1	8				1	3		2	13
22-31						10								10
22-37					1	1							1	1
23-21						2								2
23-25					1	9	3	3					4	12
23-34					1	3							1	3
24-31						9								9
27-31						1						1		2
29-31						1								1
33-25						25								25
39-25						2								2
17: 1, 2, 5									1	2		2	1	4
1, 2, 36								4						4
13, 15								2						2
29-25	1	3					1	1					2	4
18: 1, 3, 11								1						1
13, 14			1	1		1	2	2			2		3	6
19: 1, 2, 5						5								5
1, 2, 6					1	1	1	2	2	2			4	5
22-21					1	3							1	3
22-31						18								18
26-						1								1
20: 1, 2, 6	5	5				2							5	7
23-30						1								1
24-21						2								2
29-25						1								1
33-						1								1
21: 1, 2, 5											1			1
1, 2, 5, 6						30								30
1, 2, 6	1	1	2	2	2	2	2	3	1	11			8	19
1, 2, 10					2	2		2	1	3			3	7
1, 3, 11			1	2					1	1	1		2	4
17, 20											1			1
23-25						3								3

TABLE 9.—*Continued*

Serotype	Turkeys		Chickens		Reptiles		Man		Other Animals		Other Sources		Total	
	Outbreaks	Cultures	Outbreaks	Cultures	Outbreaks	Cultures	Outbreaks	Cultures	Outbreaks	Cultures	Eggs and egg products	Water, sewage, misc.	Outbreaks	Cultures
22: 1, 2, 5, 6						1								1
13, 14							1	1					1	1
16, 17, 18											1			1
33-28						1								1
23: 24-25					2	3							2	3
25-30					1	1							1	1
33-25					2	2							2	2
24: 24-28						3	2	6					2	9
24-31						1		1						2
26-25						1								1
27-31						2								2
29-28						3								3
29-31						2								2
NM						1								1
25: 23-21						5								5
23-30						10								10
23-31						1								1
27-28					1	1						2	1	3
29-31						1								1
26: 23-21						1								1
23-25						1								1
23-30					1	3	6	7	7	116	3	3	14	132
26						1								1
29					1	1							1	1
29-30	1	1							13	13		1	14	15
32-21						6								6
32-31						2								2
33-21						1								1
33-25						21	1	1					1	22
27: 22-31						1						1		2
28: 16, 17, 18									1	2			1	2
23-25						11								11
23-28						1								1
23-30						1								1
26-28						2								2
32-28					1	2							1	2
33-31						1								1
29: 32-31						1								1
33						1								1
33-21						2								2
33-31						9								9
33-40						6								6

TABLE 9.—*Concluded*

Serotype	Turkeys		Chickens		Reptiles		Man		Other Animals		Other Sources		Total	
	Outbreaks	Cultures	Outbreaks	Cultures	Outbreaks	Cultures	Outbreaks	Cultures	Outbreaks	Cultures	Eggs and egg products	Water, sewage, misc.	Outbreaks	Cultures
5, 29: 33-21-40						6								6
30: 23-25						2								2
23-30						2								2
23-31						2								2
27-28						1								1
31: 23-25			1	1		1							1	2
32: 1, 2, 6					1	1							1	1
Totals.....	829	1404	89	135	53	452	159	229	50	207	136	71	1180	2634

adaptation or partial host adaptation similar to those exhibited by certain salmonellae remains to be determined.

The cultures from eggs and egg products were derived largely from spray-dried egg powder although cultures from shell eggs, eggwhite, eggnog, and custard were included. Cultures from the two last mentioned sources were found in connection with infections in man. The cultures from water, sewage, and miscellaneous sources were not notable. With the exception of a large number of cultures of type 10: 1, 2, 5 which were isolated from carcasses, utensils, and the environment in poultry processing plants, the cultures were from outfalls of abattoirs, raw river waters, irrigation waters, sewage, and fish meal.

The number of cultures isolated from man increased rapidly in recent years. Whereas Edwards *et al.* (15) reported only 87 cultures from man, 229 are included in table 9. The sources of the cultures from man are listed in table 11. No attempt was made to separate the cultures isolated from persons affected with acute diarrhea and gastroenteritis from those derived from patients with an enteric fever-like syndrome. Both types of illness were present in symptomatic patients from whose stools the organisms were isolated, whereas the enteric fever-like syndrome predominated among those persons who yielded positive blood cultures. In some instances the separation of the two entities would have been difficult since some patients affected with acute diarrhea were febrile for long periods. In other instances sufficient information upon which to base an opinion was not available. In one instance a person with diarrhea yielded *Salmonella typhi-murium* as well as Arizona type 7: 1, 2, 6. Two symptomatic patients from whose stools types 10: 1, 2, 5 and 15: 24-25, respectively, were isolated also harbored *Shigella flexneri*. These are the only instances in which recognized intestinal pathogens were known to be associated with Arizona types in man.

The cultures from localized infections were isolated from the following sources. One culture of type 5: 13, 14 was isolated from pus in otitis media and 1 from joint fluid of an individual affected with arthritis and osteomyelitis. Of the 7: 1, 2, 6 cultures, 11 were isolated from pleural fluid, 9 from urine, 2 from spinal fluid, 1 from conjunctivitis, and 1 each from abscesses in the brain, liver, lung, retroperitoneum, scalp, thigh, and perineum. The culture of type 7: 1, 7, 8 was found in a splenic abscess and that of 9: 13, 15 in a hepatic abscess. The culture of type 21: 1, 2, 6 was isolated from pleural fluid. Type 22: 13, 14 was isolated from cerebrospinal fluid. Blood culture also was said to be positive. Several of the persons with positive urine cultures were known to be affected with prostatitis or pyelitis. Detailed histories of most of the patients were unobtainable and usually the final outcome of the infections was not learned.

An effort was made to eliminate all duplicate

TABLE 10

Sources of cultures from animals other than turkeys, chickens, reptiles, and man

Serotype	Animal, Source of Cultures and Disease or Symptoms	Total
1, 2: 1, 2, 5	Hog, lymph node, normal	1
1, 3: 1, 2, 5	Hog, spleen	1
1, 3: 1, 3, 11	Hogs, spleen	2
1, 3: 1, 7, 8	Fly pool	1
1, 4: 1, 2, 5	Dog, intestine, diarrhea (1); hog, intestine, colitis (1)	2
1, 4: 31-33	Duck, cloacal swab, normal	1
5: 13, 14	Dogs, feces, normal (2); dog, blood (1); parrot (1)	4
5: 17, 20	Macaw, liver	1
7: 1, 7, 8	Capybara, feces, colitis (1); mink, intestine, colitis (9); pheasant, intestine, enteritis (1); duck, intestine, enteritis (2); dog, feces, diarrhea (1)	14
9: 1, 2, 5	Dog, feces, normal	1
9: 1, 3, 11	Dog, feces, normal	1
9: 17, 20	Guinea pig, injected with tissues of a kangaroo rat (1)	1
10: 1, 2, 5	Monkeys, stools, diarrhea (2); dogs, feces, normal (14); cat, feces, normal (1)	17
10: 1, 2, 6	Hog, intestine, enteritis	1
11: 16, 17, 18	Parrot, liver	1
13: 1, 2, 5	Guinea pigs, livers (inoculated with organs of a rattlesnake)	2
13: 13, 14	Canaries, livers	4
14: 1, 2, 5	Canary, liver	1
16: 22-21	Hog, anal swab, normal	1
17: 1, 2, 5	Guinea pigs, livers	2
19: 1, 2, 6	Guinea pig (1); wild rodent (1)	2
21: 1, 2, 6	Rats, intestine, normal (10); pheasant, liver (1)	11
21: 1, 2, 10	Opossum, spleen (1); dogs, feces, normal (2)	3
21: 1, 3, 11	Opossum, lung and lymph node	1
26: 23-30	Monkeys, feces (115); hog, liver (1)	116
26: 29-30	Ewe, aborted fetus (1); duodenum (1); lambs (10); swine (1)	13
28: 16, 17, 18	Wild rodents	2
Total.....		207

TABLE 11

Sources of Arizona cultures isolated from man

Serotype	Stools		Blood	Localized Infections	Total
	Asymptomatic	Diarrhea, gastroenteritis, enteric fever			
1, 2: 1, 2, 5	1	8	1		10
1, 3: 1, 2, 10		2			2
1, 4: 1, 2, 5		2	2		4
1, 4: 1, 2, 6		1			1
1, 4: 1, 3, 11		1			1
5: 1, 2, 5		3			3
5: 1, 2, 10			1		1
5: 1, 3, 11			1		1
5: 13, 14		4	1	2	7
5: 17, 20	2	1			3
7: 1, 2, 6	3	41	24	30	98
7: 1, 7, 8	1	15	2	1	19
9: 1, 2, 6		1			1
9: 1, 2, 10		1			1
9: 13, 15	1	1		1	3
9: 24-31			1		1
10: 1, 2, 5		30			30
10: 1, 2, 10		1	1		2
10: 1, 3, 11	1				1
13: 1, 2, 5		1			1
13: 13, 15		1			1
14: 1, 2, 6		1			1
15: 24-25		1			1
16: 23-25		3			3
17: 1, 2, 36	4				4
17: 13, 15	2				2
17: 29-25		1			1
18: 1, 3, 11	1				1
18: 13, 14		2			2
19: 1, 2, 6	1	1			2
21: 1, 2, 6	1	1		1	3
21: 1, 2, 10	2				2
22: 13, 14				1	1
24: 24-28	2	4			6
24: 24-31	1				1
26: 23-30	1	6			7
26: 33-25		1			1
Totals.....	24	135	34	36	229

cultures from the tables, and many cultures typed were not included. From such cases as those described by Fisher (19) and Krag and Shean (26) multiple cultures from the same individual were received over long periods. From 1 unreported case, 7 isolations of type 7: 1, 2, 6 from urine, blood, joints, and bone lesions were received. Since accurate histories of the cases usually were unobtainable it cannot be said with certainty how many infections were fatal. It

is known that fatalities were involved in 13 cases, 1 of which was a case of Hodgkin's disease in a patient with diarrhea from whose stool type 7: 1, 7, 8 was isolated. Of the 12 remaining cases, none of which were known to be affected with other diseases, 5 were infected with type 7: 1, 2, 6; 2 with type 7: 1, 7, 8; and 1 each with types 1, 2: 1, 2, 5; 1, 3: 1, 2, 10; 9: 13, 15; 10: 1, 2, 10; and 22: 13, 14.

One is impressed by the fact that 30 per cent of the Arizona cultures from man were derived from blood or from localized infections. This is a much higher percentage of such isolations than one would expect in a series of infections due to nonhost-adapted salmonellae. This situation is applicable particularly to type 7: 1, 2, 6 of which more than half the cultures came from extraintestinal sources. There would seem to be two possible explanations for this situation. One is that Arizona types are more invasive in man than is the average nonhost-adapted *Salmonella* type. The second is that the cultures from man constitute a highly selected material. It undoubtedly is true that lactose-fermenting enteric bacteria from stools are much more likely to be overlooked or discarded than similar organisms from blood cultures or from localized infections. During the earlier work on the Arizona group it was thought that the bacteria characteristically fermented lactose slowly. This misconception undoubtedly was due to the failure of the majority of persons who submitted cultures for typing to recognize lactose fermentation and thus the organisms were submitted as suspected salmonellae. It was not until Solowey (38) systematically examined the biochemical characteristics of all cultures isolated from egg powder and submitted for typing all cultures which resembled Arizona strains that it became apparent that many cultures of the group fermented lactose rapidly. This observation was confirmed by Buttiaux and Kesteloot (4) who noted that the colonies on isolation plates sometimes appeared to ferment lactose. Lately these observations were emphasized by the results of LeMinor *et al.* (28) who noted that many of the organisms produced red colonies on deoxycholate-citrate agar. It seems highly probable that many Arizona strains in stools either are being overlooked because the colonies appear to be those of lactose fermenters or because when isolated they ferment lactose rapidly. If this conclusion is valid the incidence of Arizona types in man is greater than has been recognized and the high percentage of cases in which the organisms are found in blood and localized infections is due to the fact that their presence in uncomplicated cases of diarrhea generally is not detected.

A. Outbreaks of Infection Involving Multiple Cases

Included in the cultures listed in table 9 are a number which were isolated from outbreaks of infection in man in which multiple cases occurred. Six of the cultures of the 1, 2: 1, 2, 5 type isolated from stools were derived from the outbreak of diarrhea among student nurses investigated by Verder *et al.* (quoted by Murphy and Morris (31)).

Two siblings aged 10 months and 4 years, respectively, had been infected simultaneously with type 1, 4: 1, 2, 5. The organism was recovered from the blood of both children but the source of infection was not determined. Three 5: 1, 2, 5 cultures were isolated from patients among a group of 32 affected persons. These cultures were isolated in the investigation of an outbreak of food infection. Thirty-two of 33 people who attended a meal ate cream pie and became ill. The 33rd person ate cherry pie and was not affected. The 3 cultures were isolated from 3 of a small number of the patients who were available for examination. Cultures of the same type were isolated from the pie served at the meal and from the coconut cream mix used in its preparation.

One of the 7: 1, 2, 6 cultures isolated from stools was derived from a person who was 1 of 99 cases of an outbreak of diarrhea which occurred in a state hospital. All of these persons had consumed 1 lot of eggnog from which Arizona 7: 1, 2, 6 was isolated. It is unfortunate that no further stool examinations were done in connection with the outbreak but it seems probable that the Arizona serotype was responsible for the infection. In a second hospital, 4 cases of diarrhea from which serotype 7: 1, 2, 6 was isolated occurred within a brief period. The patients resided in separate wards or cottages which were said to have no common food supply and the source of the infections was not determined. In a third hospital, 2 patients who received food from the same kitchen were affected with diarrhea and type 7: 1, 2, 6 was isolated from the stools of both. The source of the infection was not determined.

Thirteen of the 7: 1, 7, 8 cultures were isolated

from as many persons who were members of a group of 23 individuals in 5 families that developed diarrhea after eating chocolate éclairs from a single bakery. The éclairs were held without refrigeration for 5 hr before delivery. Although the incubation period in the individuals affected varied from 2 to 46 hr, the average time elapsing between consumption of the food and appearance of symptoms was approximately 24 hr. The symptoms reported were abdominal cramps, nausea, vomiting, and diarrhea and in addition some persons were affected with headache, chills, and weakness. The symptoms persisted for 2 to 5 days. None of the suspected éclairs was available for examination.

Of the 30 cultures of the 10: 1, 2, 5 type isolated from diarrhea, 10 were isolated from the 2 outbreaks of infection described by Murphy and Morris (31). A third outbreak of diarrhea due to serotype 10: 1, 2, 5 involved at least 5 families and an unknown number of persons. These families had eaten uncooked banana ice cream and peach ice cream from both of which type 10: 1, 2, 5 was isolated. Cultures received from 6 of the affected persons were identified as the same type. Nothing was learned of their clinical condition other than that they were affected with diarrhea. It is of interest that this outbreak occurred in North Carolina where type 10: 1, 2, 5 long has been known to be prevalent in chickens. Many cultures of this type isolated from chickens and from the environment of poultry processing plants were received from North Carolina.

Type 10: 1, 2, 5 was isolated simultaneously from the stools of 2 siblings affected with diarrhea. The ages of the children were not stated and the source of the infection was not established.

Type 24: 24-28 was isolated from 4 patients in the same ward of a hospital within a period of 4 days. An infant with diarrhea whose sibling had been similarly affected but had not required hospitalization, was admitted to the ward. The following day 2 additional infants developed severe diarrhea. Cultures from all 3 infants yielded type 24: 24-28. Three days later the organism was isolated from the stool of a 15-year-old boy who did not develop diarrhea.

In addition to the above outbreaks in which Arizona types were isolated from the patients involved and in some instances from food as well, cultures were isolated and identified from foods thought to be responsible for extensive outbreaks of diarrheal disease in which no cultures were taken from persons affected. One culture of Arizona 7: 1, 2, 6 was recovered from uncooked turkey of a lot of birds thought to have given rise to an outbreak of diarrhea that affected some 200 individuals following a common meal. In other instances types 1, 4: 1, 2, 5 and 10: 1, 3, 11, respectively, were isolated from 2 samples of ice cream suspected of causing diarrhea in a number of consumers.

B. Observations Concerning Certain Serotypes

Edwards *et al.* (16) described briefly the histories of the cultures of all the Arizona serotypes then recognized. Edwards *et al.* (15) summarized the information available concerning the cultures from man described in their publication. Since the numbers of cultures from both animals and man have increased so markedly, it obviously is impossible to record such details. Nevertheless, some remarks concerning serotypes which have figured prominently in the development of knowledge of the group seem justified.

Types 1, 3: 1, 2, 5 and 1, 4: 1, 2, 5 previously were among the more frequently occurring types in the group, the latter being the type most often recognized. These types were being disseminated by 2 turkey hatcheries in California that later replaced their supply flocks from noninfected stock. The increase in numbers of these types has not kept pace with the group as a whole. Only 1 culture of type 1, 3: 1, 2, 5 has been recognized since 1947 and the number of cultures of type 1, 4: 1, 2, 5 has increased by less than 50 per cent, whereas the group as a whole has increased almost 600 per cent. Type 5: 13, 14 has increased only moderately in numbers but has been found in a greater variety of animals and in man. Type 5: 17, 20, although still not one of the most frequently occurring types, is represented by 61 cultures, whereas previously only 1 culture was found. The majority of these cultures came from turkey poults hatched in California or from poults hatched in Minnesota from eggs from a single source in California.

Type 7: 1, 2, 6 is notable since the number of cultures recognized increased from 4 in 1947 to 473 at present. This type is exceptional also because of the frequency of its occurrence and because it is invasive in man. In 1947 type 7:

1, 2, 6 had been recognized in but one flock of turkeys. No further eultures were recognized until 1949 when a culture from man was received. The next isolations were from man and turkeys in 1952. All these infections occurred in California and since 1952 the organism has been isolated more frequently from turkeys in California than any other Arizona type. The type was isolated from poults in Minnesota and New Jersey in 1953 and in both instances the birds were hatched from California eggs. This serotype now is widely distributed in turkeys throughout the United States. In spite of the nationwide distribution of type 7: 1, 2, 6 in fowls, with 6 exceptions, the 98 cultures from man were isolated in California. Three strains were isolated in Oregon and 1 each in New York, North Carolina, and Ontario. These circumstances indicate that the bacterium probably was not recognized in most areas.

Type 7: 1, 7, 8 was found frequently prior to 1947 and was the serotype which appeared most frequently in the present series, comprising almost one fourth of the cultures studied. However, the relative rates of isolation of types 7: 1, 2, 6 and 7: 1, 7, 8 changed markedly in recent years. Within the past 4 years, type 7: 1, 2, 6 was recognized in 334 outbreaks of infection from which 341 cultures were identified, whereas type 7: 1, 7, 8 was found in 173 outbreaks represented by 299 cultures. This reversal of relative numbers well illustrates the gradual change in incidence of serotypes which so often has been observed among the salmonellae. The histories of the cultures of type 7: 1, 7, 8 isolated from turkeys were most instructive. In 1947, 24 outbreaks of infection in poults had been observed. In most of these outbreaks the poults were hatched from eggs produced by a single cooperative turkey breeders association in California. In the present series, cultures from 408 outbreaks of infection were included and these, almost without exception, were traceable directly or indirectly to the same source. This type now is found in turkeys throughout the United States.

In contrast to type 7: 1, 2, 6, for many years type 7: 1, 7, 8 was not found among cultures from man and it seemed that the organism had little or no tendency to produce disease in man. Recently, however, it was found in the well defined outbreak of diarrhea in which chocolate éclairs were involved and has been isolated from blood and abscesses of the internal organs. Again, with one exception the cultures isolated from man originated in California. One culture was isolated in Minnesota, where the type occurs with unusual frequency in turkeys. It still is not clear why type 7: 1, 2, 6 occurs so much more frequently than type 7: 1, 7, 8 in human infections.

Type 10: 1, 2, 5 is also worthy of note. Up to 1947 only 4 cultures of this type had been found, of which 1 was isolated from a child with acute colitis. It is now represented by 192 cultures from 73 outbreaks of disease, and has continued to appear in man. Of the original 4 cultures, 1 fermented lactose and the other 3 did not. Of the 188 cultures recognized since that time only 1 fermented lactose, even after prolonged serial transfer. Otherwise, they were typical Arizona cultures. The characteristic failure of this type to ferment lactose probably was due, in part at least, to the fact that the majority of the cultures were of one enzootic type which originated from the source mentioned below.

Although this type occurred very rarely in turkeys, 50 per cent of the cultures were isolated from chickens. The epizootiology of serotype 10: 1, 2, 5 in chickens is fairly clear. A very large breeding flock in North Carolina harbored this type. Eggs from this flock were sold to hatcheries in Indiana which used them to establish supply flocks. Chicks hatched from eggs from these supply flocks were sold throughout the Southeastern States. Many of these chicks were infected with serotype 10: 1, 2, 5. Eggs from the North Carolina flock sent directly to Georgia also resulted in chicks infected with this type, which is now widely distributed in the Southeastern States and has appeared in man, dogs, and cats as well as in chickens. It will be recalled that it was this type which was found by Murphy and Morris (31) in 2 outbreaks of infection of man in Georgia. More recently an outbreak involving multiple cases occurred in North Carolina. Unlike types 7: 1, 2, 6 and 7: 1, 7, 8, of which most cultures from man originated in California, almost all 10: 1, 2, 5 infections in both animals and man either have occurred in the Southeastern States or have resulted from the secondary focus of infection established in Indiana.

The large number of cultures of type 26: 23-30 was due almost entirely to its repeated appearance in monkeys where it often was found in animals that yielded shigellae or salmonellae in addition.

Type 26: 29-30 was notable only because of its close association with sheep and its occurrence in those animals in several parts of the United States and Europe.

V. COMMENT

From the foregoing it is hoped that it has been made evident that the cultures described form a rather compact biochemical group which is composed of a series of interrelated serologic types and that the Arizona group constitutes a distinct and valid entity within the family *Enterobacteriaceae*. It is unfortunate that the organisms often have been referred to as paracolon bacteria, a designation which, when used in the unmodified sense, is so vague as to be practically without meaning. Even if it is granted that the term "paracolon" has a justifiable place in modern bacteriological usage, it cannot be applied properly to the Arizona group which, like other groups of enteric bacteria that characteristically ferment lactose, is made up of otherwise typical units which may attack lactose rapidly, slowly, or not at all.

The long-held view that enteric pathogens could be distinguished by cultivation on media containing lactose undoubtedly has been responsible for failure to isolate many Arizona strains which rapidly fermented lactose. As a result, it is not known whether the cultures that ferment lactose slowly, which constitute the majority of the cultures described here, really compose the major portion of the Arizona group or whether we are dealing largely only with the slow lactose-fermenting members of a group which characteristically ferments the sugar rapidly. From the studies of Solowey (38) on egg powder and of LeMinor *et al.* (28) on snakes, it is evident that when cultures are selected without regard to lactose fermentation, the majority of Arizona strains recognized among the isolates ferment lactose promptly. Thus, at present it is impossible to make any accurate statement regarding the incidence of members of the Arizona group in normal and diseased individuals. It can be said only that they have been isolated from man and warm-blooded animals under circumstances which strongly indicate their etiologic importance in a variety of clinical conditions.

The writers have avoided erecting a genus which would take its place in formal classifications but there is no doubt that the Arizona group stands on a par with the genus *Salmonella* and the *Citrobacter* (*Escherichia freundii*) group and should be included in any formal classification of the *Enterobacteriaceae*.

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