Survey of Infectious Multiple Drug Resistance Among
Salmonella Isolated from Animals in
the United States

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Salmonella cultures were obtained from outbreaks of animal disease from 37 states and 1 territory. They were screened for resistance to 11 antimicrobial drugs. Of the 1,251 strains studied, 935 were resistant to one or more of these agents. The three most common resistance patterns were ampicillin, dihydrostreptomycin, sulfathinoxypyridazine, tetracycline; ampicillin, dihydrostreptomycin, sulfathinoxypyridazine; dihydrostreptomycin, sulfathinoxypyridazine, tetracycline. Resistance transfer was demonstrated on 267 multiply resistant cultures, of which 181 were able to transfer all or part of their resistance pattern to a drug-sensitive recipient.

The occurrence of transferable drug resistance of the kind mediated by plasmids, called R factors, has been extensively documented since it was first demonstrated in Japan in 1959. These reports from abroad (2, 3, 5, 6, 11, 12) and the United States (7–10, 15–17, 21) are primarily studies of the phenomenon in human beings and show that it is widespread. Less information is available about the incidence of this type of resistance in animal populations. Smith and Halls (20) studied Escherichia coli strains isolated from healthy humans, calves, pigs, and fowls; although the survey was limited, their results indicated that infective resistance is probably the most common form of drug resistance among these organisms in Great Britain. Walton's investigation (22) of E. coli strains also collected from healthy animals in England led him to conclude that infectious drug resistance has wide distribution in this species in the gut of healthy pigs and calves. He correlated isolation of infectious, multiply resistant strains of intestinal coliforms with types of drugs supplied to the animals.

Smith (18) expanded his investigations to diseased animals (and humans) with an examination of pathogenic E. coli isolated from cases of human neonatal diarrhea, from calves and lambs suffering from neonatal diarrhea or bacteremia, from pigs with neonatal or postweaning diarrhea or bowel edema, and from fowls with "coli- septicemia." He found a high incidence of drug resistance with complex patterns and mostly of the infective type.

Aden and co-workers (1) noted that their 1969 study was the first on the incidence of transferable drug resistance in domestic animals in this country. They examined Enterobacteriaceae obtained from cases of neonatal diarrhea in calves and piglets and showed that this type of drug resistance was common among their cultures. In our survey of Salmonella serotypes, we found a high incidence of antimicrobial drug resistance and corresponding resistance-transfer factor.

MATERIALS AND METHODS

Between April 1968 and March 1970, 1,251 serologically identified cultures of Salmonella were received. They had all been isolated from cases of animal disease in 37 states and 1 territory a few weeks prior to our laboratory accession. The transmitting laboratories selected the cultures to include a wide variety of Salmonella and host species as possible.

Antimicrobial sensitivity patterns were determined by a standardized single-disc method (4) at the following levels: ampicillin, 10 μg; dihydrostreptomycin, 10 μg; cephalothin, 30 μg; sulfathinoxypyridazine, 0.25 mg; cillin, 10 μg; chloramphenicol, 30 μg; furazolidone, 100 μg; neomycin, 30 μg; polymyxin B, 300 units; tetracycline, 30 μg; and nalidixic acid, 30 μg.

As a matter of practicality, only cultures which showed resistance to three or more drugs were examined for transferable resistance by the technique of Schroeder et al. (15) which utilized as recipient an E. coli (083:k untypable: H14) mutated to high nalidixic acid resistance. A modification by these workers in later studies uses dicloxacillin also in the selective media for conjugation experiments.

RESULTS

Table 1 lists geographical distribution of Salmonella species with their animal sources and numbers of drugs in resistance patterns. Screening
| Salmonella serotypes (61) | No. of states represented | Animal source | No. of serotypes resistant to no. of drugs | Resistance transfer |
|--------------------------|--------------------------|---------------|-------------------------------------------|--------------------|
|                          |                          |               | 0 | 1 | 2 | 3 | 4 | 5 | >5 | Complete | Partial | None |
| S. alachua (2)           | 2                        | Chicken 1, pig 1 | 2 |   |   |   |   |   |   |          |        |      |
| S. albany (7)            | 3                        | Chicken 1, horse 1, turkey 5 | 1 | 4 | 2 |   |   | 1 | 1 |          |        |      |
| S. amager (1)            | 1                        | Pig 1         |    |   |   |   |   |   |   |          |        |      |
| S. anatum (40)           | 11                      | Chicken 4, cow 3, pig 18, turkey 15 | 4 | 15 | 11 | 9 | 1 | 2 | 6 | 2        |        |      |
| S. bareilly (2)          | 2                        | Pig 2         | 2 |   |   |   |   |   |   |          |        |      |
| S. berta (1)             | 1                        | Pig 1         | 1 |   |   |   |   |   |   |          |        |      |
| S. binza (1)             | 1                        | Pig 1         | 1 |   |   |   |   |   |   |          |        |      |
| S. blockley (15)         | 5                        | Chicken 9, pig 4, turkey 2 | 10 | 5 |   |   |   |   |   |          |        |      |
| S. braenderup (1)        | 1                        | Pig 1         | 1 |   |   |   |   |   |   |          |        |      |
| S. bredeney (17)         | 6                        | Chicken 6, pig 5, turkey 6 | 8 | 7 | 2 |   |   |   |   |          |        |      |
| S. california (5)        | 6                        | Chicken 4, turkey 1 | 4 |   |   |   |   |   |   |          |        |      |
| S. cerro (2)             | 1                        | Chicken 1, pig 1 | 1 |   |   |   |   |   |   |          |        |      |
| S. chester (13)          | 4                        | Chicken 2, turkey 11 | 7 | 2 | 3 |   |   |   |   |          |        |      |
| S. choleraeus (6)        | 1                        | Pig 6         | 6 |   |   |   |   |   |   |          |        |      |
| S. choleraeus var. kunzendorf (340) | 25                  | Chicken 1, pig 339 | 6 | 117 | 179 | 33 | 5 |   | 7 | 18 | 13 |
| S. cubana (6)            | 5                        | Chicken 2, pig 2, turkey 2 | 5 |   | 1 |   |   |   |   |          |        |      |
| S. derby (53)            | 18                       | Chicken 3, cow 4, pig 38, quail 1, turkey 6, sheep 1 | 22 | 16 | 10 | 4 | 1 |   | 1 | 4        |        |      |
| S. drypool (3)           | 3                        | Cow 1, pig 2   | 1 | 2 |   |   |   |   |   |          |        |      |
| S. eimsbuettel (15)      | 3                        | Chicken 6, cow 2, pig 5, turkey 2 | 5 | 10 |   |   |   |   |   |          |        |      |
| S. enteritidis (34)      | 7                        | Chicken 2, cow 1, duck 1, horse 1, pig 11, turkey 18 | 32 | 1 | 1 |   |   |   |   |          |        |      |
| S. give (6)              | 5                        | Chicken 1, pig 5 | 4 | 2 |   |   |   |   |   |          |        |      |
| S. heidelberg (89)       | 17                       | Chicken 18, cow 1, horse 5, pig 19, turkey 46 | 21 | 24 | 25 | 9 | 9 | 1 | 3 | 7 | 9 |
| S. indiana (1)           | 1                        | Turkey 1       | 1 |   |   |   |   |   |   |          |        |      |
| S. infantis (40)         | 13                       | Anteater 1, chicken 17, cow 3, horse 2, pig 14, turkey 3 | 26 | 11 | 1 | 1 | 1 |   | 2 |          |        |      |
| S. java (2)              | 2                        | Pig 2         | 2 |   |   |   |   |   |   |          |        |      |
| S. javiana (2)           | 2                        | Pig 2         | 1 | 1 |   |   |   |   |   |          |        |      |
| S. johnneshburg (2)      | 1                        | Chicken 1, turkey 1 | 2 |   |   |   |   |   |   |          |        |      |
| S. kentucky (2)          | 2                        | Pig 1, turkey 1 | 1 | 1 |   |   |   |   |   |          |        |      |
| S. kotibus (8)           | 3                        | Chicken 6, pig 2 | 5 | 2 | 1 |   |   | 1 |   |          |        |      |
| S. lexington (1)         | 1                        | Turkey 1       | 1 |   |   |   |   |   |   |          |        |      |
| S. litchfield (1)        | 1                        | Pig 1         | 1 |   |   |   |   |   |   |          |        |      |
| S. livingstone (1)       | 1                        | Turkey 1      | 1 |   |   |   |   |   |   |          |        |      |
| S. lomita (1)            | 1                        | Pig 1         | 1 |   |   |   |   |   |   |          |        |      |
| S. london (1)            | 1                        | Turkey 1      | 1 |   |   |   |   |   |   |          |        |      |
| S. manhattan (3)         | 2                        | Turkey 3      | 2 | 1 |   |   |   |   |   |          |        |      |
| S. miami (3)             | 2                        | Horse 1, pig 2 | 3 |   |   |   |   |   |   |          |        |      |
| S. minnesota (4)         | 2                        | Chicken 1, pig 3 | 1 | 3 |   |   |   | 2 |   |          |        |      |
| S. montevideo (10)       | 6                        | Chicken 3, pig 4, turkey 3 | 5 | 2 | 1 | 1 | 1 |   | 2 |          |        |      |
| S. munchen (13)          | 4                        | Chicken 1, goose 1, pig 8, turkey 3 | 10 | 1 | 2 |   |   |   | 2 |          |        |      |
| S. muenster (1)          | 1                        | Horse 1       | 1 |   |   |   |   |   |   |          |        |      |
| S. newington (4)         | 4                        | Chicken 1, pig 1 | 2 | 1 | 1 |   |   | 1 |   |          |        |      |
| S. newport (24)          | 12                       | Cat 1, chicken 1, cow 7, pig 14, turkey 1 | 13 | 1 | 5 | 2 | 3 | 1 | 3 | 1        |        |      |

* Total for states: Alabama 1, Arizona 3, Arkansas 38, California 1, Colorado 2, Delaware 4, District of Columbia 1, Florida 22, Georgia 4, Illinois 156, Indiana 283, Iowa 63, Kansas 1, Kentucky 18, Louisiana 19, Maryland 38, Massachusetts 3, Michigan 15, Minnesota 203, Mississippi 19, Missouri 31, Nebraska 20, New Hampshire 2, New Jersey 2, North Carolina 46, North Dakota 3, Ohio 50, Oklahoma 14, Pennsylvania 2, Puerto Rico 6, Rhode Island 1, South Carolina 38, South Dakota 8, Tennessee 15, Texas 106, Virginia 1, Washington 1, Wisconsin 11. Animals: Anteater 1, cat 1, chicken 150, cow 90, dog 1, duck 2, goose 4, horse 20, pig 678, pigeon 3, quail 2, turkey 292, sheep 7.
Table 1—Continued

| Salmonella serotypes (61) | No. of states represented | Animal source | No. of serotypes resistant to no. of drugs | Resistance transfer |
|---------------------------|---------------------------|---------------|------------------------------------------|---------------------|
|                           |                           |               | 0 | 1 | 2 | 3 | 4 | 5 | >5 | Complete | Partial | None |
| S. orion (3)              | 5                         | Chicken 1, pig 1, turkey 1 | 2 | 1 | 1 |   |   |   |   |         |         |     |
| S. oranienburg (2)        | 1                         | Pig 1         | 1 | 1 |   |   |   |   |   |         |         |     |
| S. panama (1)             | 1                         | Pig 1         | 1 | 1 |   |   |   |   |   |         |         |     |
| S. phoenix (1)            | 1                         | Pig 1         | 1 | 1 |   |   |   |   |   |         |         |     |
| S. poona (1)              | 1                         | Pig 1         | 1 | 1 |   |   |   |   |   |         |         |     |
| S. reading (10)           | 7                         | Chicken 1, pig 1, pigeon 1, turkey 7 | 4 | 4 | 1 | 1 |   |   |   |         |         |     |
| S. saint paul (96)        | 18                        | Chicken 10, cow 4, horse 1, pig 8, turkey 73 | 27 | 32 | 23 | 6 | 5 | 2 | 1 | 8 | 4 | 2 |
| S. san diego (21)         | 6                         | Goose 1, turkey 20 | 4 | 8 | 1 | 7 | 1 |   |   | 4 | 1 | 3 |
| S. schwarzengrund (6)     | 6                         | Chicken 1, pig 2, turkey 3 | 4 | 2 |   |   |   |   |   |   |   |   |
| S. senftenberg (31)       | 4                         | Chicken 1, pig 3, turkey 5 | 10 | 4 | 7 | 7 | 3 |   |   | 1 | 1 | 8 |
| S. sieburg (2)            | 2                         | Chicken 2     | 1 | 1 |   |   |   |   |   |   |   |   |
| S. taksony (1)            | 1                         | Turkey 1      | 1 |   |   |   |   |   |   |   |   |   |
| S. tennessee (7)          | 5                         | Chicken 3, pig 2, turkey 2 | 2 | 2 | 5 |   |   |   |   |   |   |   |
| S. thomsonville (6)       | 1                         | Chicken 2, cow 2, pig 1, sheep 1 | 1 | 2 | 5 |   |   |   |   |   |   |   |
| S. typhimurium (223)      | 25                        | Chicken 9, pig 7, turkey 2 | 10 | 8 |   |   |   |   |   |   |   |   |
| S. typhimurium var. copenhagen (29) | 15 | Chicken 14, cow 59, dog 1, goose 2, horse 7, pig 115, turkey 21, sheep 4 | 32 | 25 | 29 | 28 | 87 | 19 | 3 | 46 | 52 | 39 |
| S. typhimurium (126)      | 9                         | Chicken 9, cow 2, duck 1, horse 1, pig 12, pigeon 1, turkey 2, sheep 1 | 9 | 12 | 2 | 3 | 1 | 2 |   | 2 | 4 |   |
| S. typhimurium var. kunzendorf (11) | 1 | Pig 1       | 1 |   |   |   |   |   |   |   |   |   |
| S. worthington (9)        | 5                         | Chicken 2, cow 1, pig 2, pigeon 1, quail 1, turkey 2 | 5 | 2 | 1 | 1 |   |   |   |   |   |   |
| Total (1,251)             |                           |               | 316 | 355 | 313 | 116 | 119 | 28 | 4 | 79 | 102 | 86 |

for antimicrobial sensitivity showed that 25% of the cultures were completely sensitive to the spectrum, 75% were resistant to one or more drugs, 46% were resistant to two or more drugs, and 21% were resistant to three or more drugs. The last group consisted of 267 cultures divided among 22 Salmonella species. Among the multiply resistant cultures, 137 were S. typhimurium and 38 were S. choleraesuis var. kunzendorf. In the group tested for resistance transfer, resistance was most common for dihydrostreptomycin (DS), 96%, followed by sulfamethoxypyridazine (KY), 83.8%; tetracycline (TE), 77.9%; and ampicillin (AM), 69.6%. No resistance was found to chloramphenicol, furazolidone, polymyxin B, or nalidixic acid. The other drugs fell into 24 different patterns with varying transferability (Table 2). Resistance patterns encountered most often were AM, DS, KY, TE appearing 82 times with 68.2% complete or partial transfer; AM, DS, KY (39) with 84.6% transfer; and DS, KY, TE (32) with 71.8% transfer. S. typhimurium transferred completely or partially 71% of the time and S. choleraesuis var. kunzendorf 65% of the time, compared to 67% transfer for all multiply resistant cultures.

DISCUSSION

Within our specified criteria, the survey shows a higher incidence of multiply resistant cultures of S. typhimurium (10.9%) than of other Salmonella serotypes, whereas the proportion of these cultures transferring resistance was only slightly more than that of the other serotypes. Earlier studies on animal and human isolates of S. typhimurium have shown a higher incidence of drug resistance for this serotype within experimental limits (13-17). S. choleraesuis var. kunzendorf was less often resistant to three or more drugs (3%) but transferred to a similar degree. The incidence of this serotype resistant to
Table 2. Drug resistance patterns and transferability

| Resistance pattern | No. of cultures | Pattern transferred | No. of cultures | Per cent transfer |
|--------------------|----------------|---------------------|----------------|------------------|
| AM, DS, CF, KY, N, TE | 4 | AM, DS, CF, KY, N, TE | 1 | 75 |
| AM, DS, CF, KY, TE | 7 | AM, DS, CF, KY, TE | 2 | 100 |
| AM, DS, CF, KY | 7 | AM, DS, CF, KY | 4 | 85.7 |
| AM, DS, KY, N, TE | 20 | AM, DS, KY, N, TE | 4 | 70 |
| AM, DS, KY, N | 1 | AM, DS, KY, N | 1 | 100 |
| AM, DS, KY, TE | 82 | AM, DS, KY, TE | 34 | 63.4 |
| AM, DS, KY | 39 | AM, DS, KY | 15 | 84.6 |
| AM, DS, N, TE | 9 | AM, DS, N, TE | 5 | 66 |
| AM, DS, N | 4 | AM, DS, N | 1 | 33 |
| AM, CF, KY, TE | 1 | AM, CF, KY | 1 | 0 |
| AM, CF, TE | 1 | AM, CF, TE | 1 | 0 |
| AM, KY, N, TE | 1 | AM, KY, N | 1 | 100 |
| AM, KY, TE | 6 | AM, KY, TE | 2 | 50 |
| AM, KY, N | 1 | AM, KY, N | 1 | 100 |
| DS, CF, KY | 2 | DS, CF, KY | 1 | 0 |
| DS, CF, CL | 1 | DS, CF, CL | 1 | 0 |
| DS, KY, CL, N, TE | 1 | DS, KY, CL, N, TE | 1 | 100 |
| DS, KY, CL | 1 | DS, KY, CL | 1 | 0 |
| DS, KY, N, TE | 18 | DS, KY, N, TE | 5 | 66 |
| DS, KY, N | 1 | DS, KY, N | 1 | 0 |
| DS, KY, TE | 32 | DS, KY, TE | 9 | 71.8 |
| DS, N, TE | 23 | DS, N, TE | 8 | 60 |

* AM = ampicillin, DS = dihydrostreptomycin, CF = cephalothin, KY = sulfamethoxypyridazine, CL = colistin, N = neomycin, TE = tetracycline.
two or more drugs is higher than that for S.
	typhimurium.

The strains of Salmonella studied were ap-
parently invasive pathogens responsible for
disease conditions and mortality. The mortality
rate as obtained from the partial histories of these
disease outbreaks indicates that 7,482 head of
livestock, principally pigs and cattle, and 59,241
birds (including turkeys, chickens, geese, and
ducks) died. Many history sheets were not com-
plete in that the numbers of animals dead were
given at the time of sample collection, and final
mortality rate could not be obtained. The figures
represent only a portion of actual deaths. There
was no provision for recording treatment of ill-
ness; thus, we are unable to correlate incidence
of resistance with use of antimicrobial drugs.

A recent study (19) of in vivo transfer of
antibiotic resistance among organisms isolated
from chickens, calves, and pigs shows that many
factors are involved in resistance transmission,
particularly the ability of organisms to colonize
the alimentary tract. The presence of a clinical
syndrome in the animals from which the Sal-
monella strains of this survey were isolated would
indicate that this requisite condition was met.

This survey indicates that pathogenic sal-
monellae with infectious multiple resistance have
been present in numerous outbreaks of disease
in the animal populations of the United States.

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