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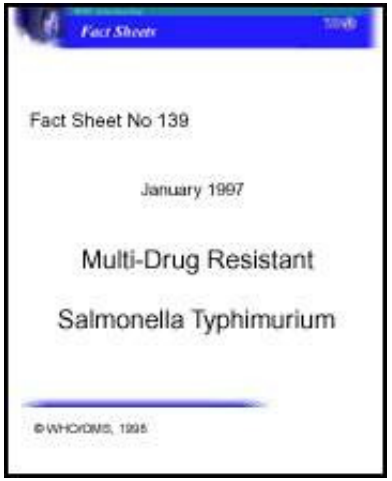

Fact sheet No 139: Multi-Drug Resistant Salmonella Typhimurium - January 1997 (WHO, 1997, 3 p.)

(introduction...)

MULTI-DRUG RESISTANT SALMONELLA TYPHIMURIUM

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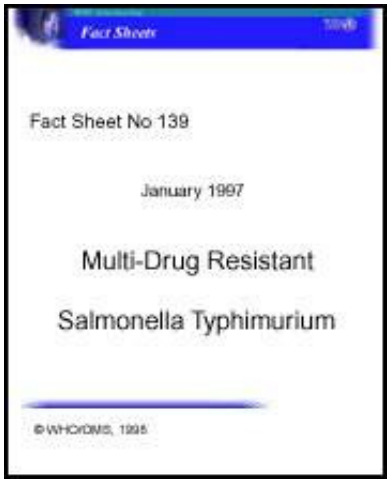

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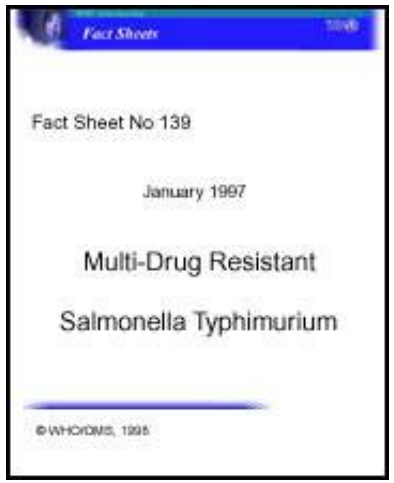

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- **MULTI-DRUG RESISTANT SALMONELLA TYPHIMURIUM**

MULTI-DRUG RESISTANT SALMONELLA TYPHIMURIUM

It was in 1885 that Daniel E. Salmon, U.S. veterinary surgeon, discovered the first strain of Salmonella. Today, there are 2213 known strains and the book is not closed. Over the years, antibiotic resistant strains have developed that are difficult to control and there is a body of evidence in the scientific literature suggesting the possibility that some of these strains may have emerged due to use of antibiotics in intensive animal husbandry. Recent years saw a dramatic rise both in terms of incidence and severity of cases of human salmonellosis; compared to 1980 some countries in Europe witnessed a staggering 20-fold increase in incidence in the last 10 - 15 years. Where the epidemic has been further studied, the majority of cases has been caused by strains or, more correctly, serotypes of *Salmonellosis enteritidis and Salmonellosis typhimurium*. The bad news is that since the beginning of the 1990s, strains of *S. typhimurium*, which are resistant to a range of antibiotics, have emerged and are threatening to become a serious public health

problem. This is part of a general trend. The incidence of bacterial resistance has increased at an alarming pace in recent years and is expected to continue rising at a similar or even greater rate in the future as antimicrobial agents or antibiotics lose their effectiveness.

SALMONELLOSIS

Transmission: Salmonellosis in humans is contracted mainly through the consumption of raw or undercooked contaminated food of animal origin (mainly meat, poultry, eggs and milk), although many other foods have been implicated in its transmission. The causative organisms pass through the food chain from primary production or through cross-contamination from food products in households or food-service establishments and institutions such as hospitals. In developed countries human to human transmission is uncommon but can occur, notably in institutions, for instance special-care baby units and residential homes for the elderly. Little is known about the epidemiology in developing countries but spread within hospitals and health centres has been reported.

A total of 2213 different salmonella strains have been identified. Epidemiologically, they can be classified according to their adaptation to human and animal hosts:

- **Group 1, e.g. *Salmonella typhi and Salmonella paratyphi*, causes enteric fever only in humans and in higher primates.**

- **Group 2 causes disease in certain animals: *Salmonella dublin* in cattle, *Salmonella cholerae-suis* in pigs, but only infrequently in humans.**

However, when these strains do cause disease in humans, it is often invasive and can be life-threatening.

- **Group 3 includes the remaining strains. Typically, such strains cause gastroenteritis which is often mild and self-limiting but can be severe in the young, the elderly, and patients with weakened resistance against infectious diseases. This group features *Salmonella enteriditis* and *Salmonella typhimurium*, the two most important strains for salmonellosis (transmitted from animals to humans).**

The clinical course of human salmonellosis is usually characterized by acute onset of fever, abdominal pain, diarrhoea, nausea and sometimes vomiting. In some cases, particularly in the very young and in the elderly, dehydration can become severe and life threatening. Antibiotic treatment is necessary in less than 2% of the clinical cases. Serious complications occur in a small proportion of cases. The incidence is particularly high in children and the elderly accounting for up to 60% of all reported laboratory confirmed cases. Studies in developed countries indicate that more than 80% of all salmonellosis cases occur individually rather than as outbreaks.

Cost estimates per reported case of human salmonellosis range from US$ 1

000 to $ 1 300 in North America and Europe. The annual cost of salmonellosis in the United States of America is estimated to total almost US$ 4 000 million. The United Kingdom Food and Drink Federation calculated in its 1994 report that foodborne illness, principally salmonellosis, is costing the British economy about UK 1 000 million annually. The costs associated with individual outbreaks in North

America and Europe ranged from around US$ 60 000 to more than US$ 20 million.

SALMONELLA TYPHIMURIUM

Salmonella typhimurium **can be found in a broad range of species as well as the environment. Together with** ***Salmonella enteritidis*****, it causes the overwhelming majority of cases of zoonotic salmonellosis in many countries. Because of their predominance, it is necessary to discriminate between the various serotypes in the course of epidemiological investigations and a fairly sophisticated technique called phage typing is used for this purpose in many countries.**

EMERGENCE OF MULTI-DRUG RESISTANT SALMONELLA TIPHYMURIUM DT 104

Multi-drug resistant ***Salmonella typhimurium*** **DT 104 initially emerged in cattle in 1988 in England and Wales. Subsequently, the strain has been isolated from poultry, sheep, pigs, and horses. Antimicrobial therapy is used extensively to combat Salmonella typhimurium infection in animals. The evolution of a strain resistant to the commonly-used antibiotics has made infections with** ***Salmonella typhimurium*** **in food animals difficult to control and it will likely remain an animal health problem for quite some time. To make things even worse, a particular variant of** ***Salmonella typhimurium*****, rather awkwardly called R-type ACSSuT, has developed multiple drug resistance as an integral part of the genetic material of the organism. Unlike other salmonella strains, multiresistant** ***Salmonella typhimurium DT 104*** **is therefore likely to retain its drug resistance genes even when antimicrobial drugs are no longer used.**

EPIDEMIOLOGY AND TRANSMISSION

The primary route by which humans acquire infection is by consumption of contaminated food of animal origin. Unlike *Salmonella enteritidis* which is mainly associated with poultry and eggs, multi-drug resistant *Salmonella typhimurium DT 104* can be found in a broad range of foodstuffs. Outbreaks in the United Kingdom of Great Britain and Northern Ireland have been linked to poultry, a variety of meats and meat products, and unpasteurized milk. In addition to acquiring infection from contaminated food, human cases have also occurred where individuals have had contact with infected cattle. A small proportion of cases may have contracted infection from pets such as cats and dogs, which can also be infected with this strain of Salmonella. Pets probably acquire the infection like humans, in other words through consumption of contaminated raw meat, poultry or poultry-derived products.

The evolution of specific salmonella serotypes in intensive animal husbandry and subsequently in humans has been observed over the last three decades. The most recent epidemic was caused by *Salmonella enteritidis*, which peaked in humans in 1992 in many European countries. Its current slight decline sets the scene for re-emergence of *Salmonella typhimurium* as - epidemiologically - the most important serotype in human salmonellosis. Another possible scenario is that these two particular strains of epidemic potential will dominate in many countries within foreseeable future.

GEOGRAPHIC DISTRIBUTION

England and Wales: The disease reporting system in England and Wales has revealed a ten-fold increase in the number of human cases of multi-drug resistant *Salmonella typhimurium DT 104* in the six year period 1990-1996 going from 300

to 3500 cases per year. This specific strain is second only to *Salmonella enteriditis* as the most common salmonella in humans in England and Wales in 1995 and more than 55% of cases of *Salmonella typhimurium* in humans were caused by the muilti-drug resistant DT 104. It has worked out stable resistance to some of the most common antibiotics: ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline. Since 1994, an increasing number of isolates with additional resistance to trimethoprim and a few with additional resistance to ciprofloxacin have been reported. Infection with multi-drug resistant *Salmonella typhimurium DT 104* has been associated with hospitalization rates which are twice that of other zoonotic food-borne salmonella infections and with ten times higher case-fatality rates.

Other countries: An increase in overall number and percentage of multi-drug resistant *Salmonella typhimurium DT 104* is also reported from other European countries. In Germany, it accounted for up to 10% in more than 10 000 salmonella samples from human sources examined in 1995; and 18% of those examined in 1996. Almost all DT 104 isolates were multi-drug resistant with the same resistance pattern as in England and Wales, although resistance to ciprofloxacin has not yet been observed. *Salmonella typhimurium DT 104* was recently detected in the United States but little is known about its prevalence and means of transmission. Preliminary evidence suggests that DT 104 may have spread widely in the United States during the past two to three years which may result in a marked increase in human illness in the near future. Over the past three decades, practically all countries in Europe have reported sharp rise in salmonellosis incidence. The same pattern could be observed in a number of countries in the Middle East and South-East Asia.

CONCLUSIONS

The emergence of Salmonella strains that are resistant to commonly used antibiotics is important to clinicians, microbiologists and those responsible for the control of communicable disease and to the food industry. It is also important to farmers who may sustain economic losses when consumer confidence in their products is lost. Control of multi-drug resistant Salmonella typhimurium DT 104 requires reducing infection in food animals and lowering the risk of contamination at all stages in the food production chain. In addition, the avoidance of unnecessary antibiotic usage in food animals should be combined with good husbandry, good abattoir practice and good hygiene at all stages in the food production chain from processing plants to kitchens and food service establishments.

Existing knowledge and technology cannot be used to provide consumers with pathogen-free raw meat and poultry, and it is very unlikely that the eradication of salmonellas in domestic animals is possible in the foreseeable future. The increased occurrence of drug resistant pathogens in foods of animal origin emphasizes the need for cooking foods thoroughly prior to consumption. Education of food handlers in the principles of safe food handling is an essential step towards reducing the incidence of food-borne disease resulting from cross-contamination during processing and preparation of foods. Educating farmers and their families regarding the risks of occupationally acquired infections is also an important step in the control of human infections from *Salmonella typhimurium DT 104.*

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