

The Shiga Toxin (Stx) producing E. coli O104:H4 outbreak in Europe and the paradigm shift in regard to Stx-producing E. coli as human pathogens

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An outbreak with 3842 cases of human infections with Shiga Toxin (Stx) producing, Enteroaggregative Haemorrhagic E. coli (EAHEC) O104:H4 struck Germany and other countries in Europe and overseas in May/June 2011. The high proportion of adults affected and the extreme high number of patients (22.2%) developing Haemolytic Uraemic Syndrome (HUS) makes it the most dramatic ever seen since Stx-producing E. coli (STEC) were first described as human pathogens. The characteristics of the outbreak strain, the way it spread among humans and the resulting clinical pictures have changed the way STEC are regarded as human pathogens in general. EAHEC O104:H4 and other EAHEC serotypes belong to an emerging E. coli pathotype which is endemic in Africa and has spread to Europe and Asia. Other STEC O104 strains, such as STEC O104:H2, O104:H7 and O104:H21 were implicated in outbreaks and sporadic infections of humans in different countries but these are fundamentally different from the EAHEC O104:H4 strain, as they do not possess enteroaggregative properties. EAHEC O104:H4 have evolved from enteroaggregative E. coli (EAEC) by uptake of an Stx2a encoding bacteriophage. No other virulence markers of classical enterohaemorrhagic E. coli (EHEC) including the chromosomal locus of enterocyte effacement (LEE) are present in EAHEC strains. EAHEC O104:H4 colonizes humans through AAF-pili encoded by the EAEC-plasmid. The EAHEC O104:H4 strains possess the full virulence characteristics of EAEC (aatA, aggA/agg3A, aggR, aap, set1 and pic). The AAF colonization mechanism substitutes the LEE functions for bacterial adherence and delivery of Stx2a into the human intestine resulting clinically in HUS. Humans are the only known natural reservoir for EAEC and EAHEC. In contrast, classical STEC and EHEC are associated with animals as natural hosts. Contaminated sprouted seeds produced in Northern Germany were identified as vehicle of transmission of the EAHEC O104:H4 outbreak strain. Secondary transmission of the pathogen from human to human and human to food/environment was found important. Epidemiological investigations revealed EAHEC O104:H4 contaminated fenugreek seeds as the source of entry of the agent into the food chain. However, microbiological investigations of seeds and sprouts grown from fenugreek seeds were negative. The survival of EAHEC in seeds and the frequency of human carriers of EAHEC need to be explored for a better understanding of EAHEC transmission routes.