by Peleg and colleagues [2] should alert policy makers to these issues.

The scale of damage and the immense organizational and logistic challenges encountered in a major earthquake require a national plan for emergency response. A governmental planning committee is now finalizing a national response plan for earthquake mitigation and emergency response. This committee includes senior representatives of all ministries and related bodies. It has presented a plan, which if implemented, would substantially reduce the loss of life and property. It recommends strict adherence to land zoning and building codes, retrofitting of housing in residential areas—which does not comply with present standards, and the organization of emergency response and training of communities in high risk areas. The authors call for measures to ensure that medical facilities, particularly hospitals, will continue to function after major disasters. There is no alternative to a hospital for ensuring proper surgical care of trauma victims.

A medical subcommittee appointed by the Ministry of Health has presented a national health plan for earthquakes. Recommendations include: command and control of operations, medical treatment of earthquake-related injuries, hospital preparedness, community and primary health response, public health support, rehabilitation of victims, psychological stress management, retrofitting of buildings and infrastructures in medical facilities, international assistance, and the necessary budgets.

In conclusion, Israel has had its share of mass casualties, due chiefly to wars and terrorist activities. There is, however, no guarantee that a major disaster—caused by a large aircraft crash or an earthquake—will not occur in the near future. Preparedness for such events is imperative and requires the mobilization and full cooperation of all emergency services, including the health services.

References

Correspondence: Dr J. Adler, 18A Kubovy St., Jerusalem, 96757, Israel.
Phone: (972-2) 641-2435
Fax: (972-2) 642-9162
email: jaadler@netvision.net.il

---

**Probiotics – An Important Therapeutic Concept Awaiting Validation**

Emanuel Lebenthal MD and Yael Lebenthal MD

1 Department of Pediatrics, Hadassah University Hospital, Mount Scopus, Jerusalem, Israel
2 Division of Pediatric Endocrinology, Diabetes, and Metabolism, Schneider Childrens Medical Center, Petah Tiqva, Israel

*Key words:* probiotics, *Lactobacillus*, microbial balance, colonocyte, vaginosis

The concept that lactobacilli might be useful in displacing and replacing harmful microorganisms on mucosal surfaces was presented a century ago [1]. Three decades ago, it was suggested that probiotics constitute the other half of the antibiotic story [2], and was defined as organisms and substances that contribute to a better intestinal microbe balance [2]. Later, probiotics was defined as a live microbial food supplement that beneficially affects the host animal by improving its intestinal microbial balance [3]. The definition was broadened to include microorganisms that benefit humans or animals by improving the properties of the indigenous microflora [4]. A still later definition emphasized living microorganisms, which upon ingestion in certain numbers, exert health benefits beyond the inherent basic nutrition [5]. Currently, probiotics is broadly defined as the preparation of a product containing viable, defined microorganisms in sufficient numbers that alter the microflora by implantation or colonization in a compartment of the host and exert beneficial health effects in the host [6].

The complex gut ecosystem is inhabited by 50 genera and over 400 separate microbial species [7]. More than 75% of the wet weight of fecal output is composed of bacterial cells, each gram containing approximately $1 \times 10^{11}$ microbes [7]. The microbial community differs in composition along the length of the gut, with the colon containing increased numbers of indigenous microbes [7]. Relatively, the large intestine contains the most complex and diverse microbial populations [7]. The microbes are comprised of rapidly transmitting and relatively persistent bacteria [8]. The physiologic environments of the microbes vary from acid conditions in the stomach to an alkaline pH in the small bowel, in addition to changes in motility, sloughing of epithelial cells, epithelial mucus secretions and secretions of bile, exocrine pancreas, gut-associated lymphatic cells and secretory immunoglobulins [9]. The gut microflora is metabolically adaptable and is dependent on the availability of substrates like carbohydrates [10].

An important energy source for the colonocyte is short chain fatty acids (acetate, propionate and butyrate) produced from colonic microbial fermentation of undigested complex carbohydrates [11]. The competition among bacteria for nutrients and space contributes to the microbial composition of the ecosystem. One of the theoretic considerations for adding probiotics such as...
Lactobacillus acidophilus is its supply of short chain fatty acids as the main luminal energy source for the colonocyte [12]. A second theoretic consideration is its provision of a salvage pathway for lactose malabsorption and intolerance, through hydrolysis of lactose by lactobacilli in the colon, thereby ameliorating the symptoms resulting from the ingestion of dairy products [13].

In this issue of IMAI, Chermesh and Eliakim [14] discuss the concept of using probiotics for Crohn's disease and ulcerative colitis. One of the reasons for using lactobacilli in active Crohn's disease is that the gut flora is rich in Escherichia coli and depleted of bifidobacteria [15]. In their review of probiotic use in gastrointestinal disease, Chermesh and Eliakim [14] present the rationale for its application in lactose intolerance, antibiotic-associated diarrhea, viral gastroenteritis and travelers' diarrhea. One of the key questions is what kind of probiotic preparation to use. The authors cite the study of Giovannetti et al. [16], who treated chronic relapsing pouchitis with four strains of lactobacilli, three strains of bifidobacteria, and one of Streptococcus salivarius. The success of the treatment might have been due to the generation of short chain fatty acids, which provided a luminal source of energy to the enterocyte [12]. The hypothesis that correcting the bacterial imbalance causes an immune response was suggested as a mechanism of action of probiotics, but it has yet to be proven.

Also presented in the current IMAJ issue is the possible use of probiotics for other mucosal systems. Shalev [17] reviews the use of lactobacilli for bacterial vaginosis in pregnancy. Conceptually, he posits, by altering the mother's intestinal flora with probiotics we can influence the habituation of the microflora in the offspring and possibly prevent certain infections and diseases.

Nonetheless, the possibility of side effects should not be overlooked. Dunne et al. [18] articulate the prerequisites for successful probiotic use: namely, the bacteria of the human host, their non-pathogenic behavior, viability during gut passage, ability to adhere to the colonocyte, and resistance to gastric acidity, bile, pancreatic enzymes, etc. In addition, the prospect that the probiotic may produce antimicrobial substances, modulate immune response and influence metabolic activity should be considered and might be of great benefit in health and disease.

However, the picture is considerably more complex since methodologic problems arise when attempting to prove specific benefits of probiotics. There are inherent problems in the study design with regard to different probiotics. Multiple probiotic agents have been suggested and tested, but repeated studies have not yielded uniformity. Moreover, different dosing patterns of bacteria have been used in various studies. Acceptable endpoints to prove efficacy among the many study designs are rarely attainable. Finally, many uncontrolled variables are overlooked in the design of probiotic studies, yielding inconclusive results.

Premusably in the future, once we have acquired more information and a better understanding of gut microflora composition, colonization, interaction, translocation and immunomodulation, we might comprehend the probiotic effect in different diseases. It will be difficult to promote the concept of probiotic treatment without a carefully designed study – one that must include specific probiotic agents, fixed bacterial species and dosage, null hypothesis, inclusion and exclusion criteria, appropriate sample size, etc. Furthermore, based on extensive research of the human host bacteria, we might be able to develop innovative biotechnology-based probiotic products tailored to promote health and prevent specific diseases. Until then, we have an excellent preventive and therapeutic concept that has yet to be proven.

References

Correspondence: Dr. E. Lebenthal, Dept. of Pediatrics, Hadassah University Hospital, Mt. Scopus, P.O. Box 24035, Jerusalem 91240, Israel. Phone: (972-2) 584 5082 Fax: (972-2) 579 5566 email: lebenthal@yahoo.com