



Battling Cancer Through Cooperation: Israeli-Palestinian Conference on GI Oncology – From the Bench to the Bedside

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A joint Israeli-Palestinian conference on gastrointestinal cancer took place in Ramallah on April 6–7, 2000. This meeting included a summary of the research project that had been initiated 2 years previously to evaluate the epidemiological and molecular differences among Palestinians, Ashkenazi and Sephardic Jews. It also provided a broad framework for discussing international approaches to etiology, pathogenesis, detection and management of gastrointestinal cancers. Participants included 60 leading Palestinian and 50 Israeli medical professionals, as well as four international experts from the United States and Britain.

Some of the highlights of the meeting are summarized here: Prof. Levin (MD Anderson Medical Center, Texas, USA) presented an overview on the frequency of colorectal cancer (CRC). He indicated that early detection and lifestyle modifications can reduce the incidence and mortality from CRC. He stressed the importance of physical activity as a regular daily practice, a healthy diet (reduce fat to <25%, and consumption of at least five items of fruits and vegetables per day), and abstinence from smoking and alcohol. Folate, green tea, coffee and hormonal replacement therapy could be protective. Although the mortality from the disease is 50%, new treatment modalities were recently proven more efficacious than the standard 5FU/leucovorin protocols. Irinotecan (CPT 11) has been shown to be more

effective, and when taken in combination with 5FU/leucovorin provides better results than standard protocol treatment. Oxaliplatin is advocated in advanced stages of the disease.

Prof. Neugut from Columbia University in New York reported that epidemiological and molecular genetics studies have shown major similarities between small and large bowel cancer.

Prof. Dubrow (MD Anderson) demonstrated the future technology of gut imaging by virtual colonoscopy, and suggested that the next decade will witness the widespread use of this method of screening for colorectal neoplasia.

Prof. Atkin from St. Marks Hospital in London described the UK experience in screening sigmoidoscopy among more than 40,000 patients. This prospective intervention, once in a lifetime, in asymptomatic individuals at the age of 60, can reduce the incidence of CRC by 50%.

Dr. Fireman (Hillel Yaffe Hospital in Israel) reviewed the epidemiological differences in the prevalence of CRC among Israelis and Palestinians. While the disease is most common among Ashkenazi Jews (highest risk), it is found in only 25% in Sephardic Jews and in less than 10% of Israeli Arabs (only 38 cases from over 500 consecutive patients with CRC).

Dr. Karsbary (Mukassed Hospital in East Jerusalem) reported the data on CRC in the West Bank. In 1999 the

incidence was 4.8/100,000. The mean age was 62 years (range 34–82) and 10% involved the rectum. Most of them were Duke's D (45%), followed by Duke's B (42%), with only 13% Duke's B and no cases in Duke's A. The current treatment is 5FU and leucovorin, yet not all patients are able to receive more than two to three treatment sessions. He also discussed the difficulties encountered in providing appropriate chemotherapy.

Prof. Arber (Tel Aviv Sourasky Medical Center) summarized the importance of the role of non-steroidal anti-inflammatory drugs (NSAIDs) in preventing CRC. Overall, NSAIDs can reduce the incidence and mortality from CRC by 50%. However, the profile of side effects, including gastrointestinal and renal toxicity, is significant, with more than 50 deaths per day in the USA as a direct consequence of using this class of agents. Today there are two classes of promising new drugs that are devoid of such toxicity. The first is a specific COX-2 inhibitor; COX-2 is an enzyme that is up-regulated in 40–50% of colorectal adenomas and in 85% of CRC. He presented the results of a study that was conducted by Searle at MD Anderson Medical Center in Texas and St. Marks Hospital in London. This paper (*N Engl J Med*, in press) demonstrated that the administration of 400 mg b.i.d of Celebrex for 6 months decreased the number of polyps by 35%. Another promising drug is sulindac sulfone (ApotosynTM cell pathway, Horsham, PA,

USA). This is not an NSAID, as it lacks the anti-inflammatory properties and does not inhibit COX-1 or COX-2. Aptosyn™ is a selective apoptotic anti-neoplastic drug (SAAND). The underlying mechanism of action of this drug was recently discovered. It is a novel mechanism involving selective inhibition of cyclic GMP phosphodiesterase activity exclusively in neoplastic tissue and not in normal mucosa. A randomized, international, multi-center, placebo-controlled trial in the USA, the UK, Sweden and Israel was completed last year. Seventy-four patients received sulindac sulfone (150 mg q.i.d) or placebo for 12 months. The primary endpoint was the number of polypectomies. At the end of the study a reduction of approximately 50% in polyp number was noted in treated patients.

Prof. Darwish (Al-Quds University, East Jerusalem) summarized the preliminary results of a joint research program between his group and the group of Prof. Arber. Additional participants in this 2 year project were Dr. Sweidan (Augusta Victoria Hospital, East Jerusalem) and Dr. Maher (Mukassed Hospital, East Jerusalem), Dr. Trajheo and Dr. Stern (Tel Aviv Sourasky Medical Center), as well as Dr. Hibshoosh, a collaborator from Columbia University in New York. The study group comprised 39 males (52%) and 36 females (48%), with a median age of 66 years. The majority of tumors among the Ashkenazi and Sephardic Jews (about 70%) were in Duke stages A and B, while those of the

Palestinian group were in stages C and D. Similarly, tumor grade was similar in Ashkenazi Jews and Palestinians. About 70% were poorly differentiated, while almost all tumors (92%) among the Sephardic patients were well differentiated. Smoking was most common among Palestinians, and alcohol consumption was very low in all three groups. Evidently, the 5 year survival is significantly higher among the Ashkenazi Jews (70%) compared to the Sephardic Jews and Palestinians (47% and 40% respectively).

Dr. Abu-Saleh from the Palestinian Council of Health summarized the Palestinian policy in the battle against cancer. The most common malignancies are bladder, lung and CRC. The latter has a lifetime probability of only 0.7%, raising the crucial question of the efficacy of a screening program among Palestinians. Notwithstanding this figure, the initial phases of organizing surveillance and early detection programs are underway in the Palestinian Authority.

Prof. Niv, President of the Israel Society of Gastroenterology, indicated that special attention is being given toward an Israeli policy for colorectal screening. Direct help from family practitioners is extremely important. Twelve studies with more than 35,000 participants have been performed in Israel. Sigmoidoscopy was of greater significance than fecal occult blood tests. Of interest was the observation that those who refused to participate in the screen-

ing program were those at the highest risk for harboring cancer.

Prof. Bar-Meir (Sheba Medical Center, Tel-Hashomer, Israel) presented a unique and novel simulator for the use of training gastroenterologists. The system combines basic techniques that are designed for elementary training, as well as sophisticated procedures more suitable for advanced study to bolster the skills of already established physicians.

Prof. Witz (Tel Aviv University) referred to the importance of the cancer microenvironment. Metastasis occurs only when the microenvironment is favorable. Microenvironment can change mutation frequency by more than 500%.

Prof. Arber concluded the meeting by summarizing: Ashkenazi Jews have the highest rate of CRC, yet they have the best 5 year survival rate. Sephardic Jews are diagnosed at a more advanced stage, the tumors are poorly differentiated and they lack p27. Palestinians have significantly higher cyclin D1 levels, which may in fact explain the lower mortality rate among Ashkenazi Jews.

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