

**Dept. of Epidemiology
and Preventive Medicine**

**Center for the Study
of Bioterrorism**

**Research Forum on Epidemiology of
Infectious Diseases and Biosecurity**

First Meeting

10/7/2008

**School of Public Health
Sackler Faculty of Medicine
Tel Aviv University
POB 39040, Tel Aviv, Israel, 69978
Tel: +972-3-6408572, Fax: +972-3-6409868**

Program

13:00 Registration & Light Refreshments

13:30 Opening Greetings

Prof. Yoseph Mekori

Dean, Sackler Faculty of Medicine.

Prof. Mordechai Shani

Head, School of Public Health

Prof. Daniel Cohen

Head, Dept. of Epidemiology & Preventive Medicine and Director, Center for the Study of Bioterrorism

First Session

**Chairperson: Prof. Tamar Shohat, Israel Center for Disease Control
& Tel Aviv University**

14:00 Molecular and Seroepidemiological Studies to Investigate the Emergence of *Vibrio vulnificus* in Israel

Dr. Naiel Bisharat

Emek Medical Center & Dept. of Epidemiology & Preventive Medicine, Tel Aviv University

14:30 Immunosuppressive Treatments Reduce the Long Term Immunity to Smallpox

Dr. Itay Wiser

Dept. of Epidemiology & Preventive Medicine, Tel Aviv University

15:00 *Helicobacter pylori* Infection is Associated with Low Serum Ferritin Levels in Israeli Arab Children

Khitam Muhsen, MSc, PhD candidate

Dept. of Epidemiology & Preventive Medicine, Tel Aviv University

15:30 Application of Knowledge Discovery in Databases (KDD) to Define the Influence of Methicillin Resistance on the Mortality of Patients with Nosocomial *S. aureus* Bacteremia

Tomer Ziv, MHA, MBA, PhD candidate

Center for the Study of Bioterrorism & Dept. of Epidemiology & Preventive Medicine, Tel Aviv University

16:00 Coffee Break

Secound Session

Chairman: Dr. Moshe Ephros (Efrat), Carmel Medical Center & Technion

16:30 Epidemiology and vaccine-prevention of Tick-Borne Encephalitis

Dr. Pamela Rendi-Wagner

Dept of Spec. Prophylaxis & Trop. Med. Center of Physiology & Pathophysiology, Medical University Vienna, and Dept of Epidemiology and Preventive Medicine, Tel Aviv University.

17:00 Epidemiology of *Group B Streptococcal* carriage in Jewish and Arab pregnant women in northern Israel, a comparison

Dr. Moshe Ephros (Efrat)

Carmel Medical Center & Technion, Haifa

17:30 Incidence of Early Onset Neonatal Invasive *Group B Streptococcal* Disease, 2006-2007, Israel

Dr. Michal Bromberg

Israel Center for Disease Control, Tel Hashomer

17:45 Seroepidemiological studies on the immune status of the Israeli population. What can we learn from their findings?

Prof. Daniel Cohen

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18:15 Closing Remarks

Prof. Daniel Cohen

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Abstracts

MOLECULAR AND SEROEPIDEMIOLOGICAL STUDIES TO INVESTIGATE THE EMERGENCE OF *VIBRIO VULNIFICUS* IN ISRAEL

*Naiel Bisharat*¹

¹Department of Medicine D, HaEmek Medical Center, Afula, and Department of Epidemiology and Preventive Medicine, The Sackler Faculty of Medicine, Tel-Aviv University

Background: In 1996 a serious outbreak of severe soft tissue infections erupted among Israeli fish farmers and members of the general public who handled live fresh fish cultivated in inland fish farms. The responsible pathogen was a new strain of the species *Vibrio vulnificus*, named biotype 3 or the Israeli biotype of *V. vulnificus*. The reasons for the disease emergence in Israel remained largely unclear and raised several questions related to various potential risk factors.

Methods: Multilocus sequence typing and phylogenetic tools were used to investigate the genetic structure of the bacterium. Seroepidemiological studies were used to investigate the immune response to LPS of *V. vulnificus* biotype 3 and its correlation with disease susceptibility. Ecological studies were used to study the relationship between climate change and disease emergence.

Results and conclusions: At the species level, a highly virulent and genetically distinct clone emerged by genetic recombination between two non-pathogenic populations. Nucleotide sequence analysis suggested that the Israeli biotype has only recently evolved, consistent with the disease epidemiology in Israel. Occupational exposure to the emerging biotype may have protected fishermen against severe disease through acquisition of natural immunity by means of anti LPS antibodies. And lastly, global warming and the consequent change in air temperatures may have had a significant impact on the timing of disease eruption.

IMMUNOSUPPRESSIVE TREATMENTS REDUCE THE LONG TERM IMMUNITY TO SMALLPOX

Wiser I^{1,5}, Orr N.^{1,5}, Kaufman B.^{2,5}, Segev S.^{3,5}, Smetana Z.⁴, A. Bialik^{1,5}, Mendelson E.^{4,1,5}, Catane R.^{2,5}, Cohen D.^{1,5}

¹Department of Epidemiology and Preventive Medicine, School of Public Health, ²Oncology Institute and ³Infectious Diseases Unit, Sheba Medical Center, Tel Hashomer, ⁴Central Virology Laboratory, Public Health Services, Ministry of Health, Tel Hashomer, ⁵Sackler Faculty of Medicine, Tel Aviv University

Background: Mass vaccination will be the principal preventive measure if cases of smallpox will occur following an act of bioterrorism. Vaccination of subjects who received immunosuppressive therapies is problematic because of the reactogenicity of the vaccine. There is also a concern that immunity following childhood vaccinia immunization has been affected in these subjects.

Objective: To examine the effect of cytotoxic chemotherapy on long term immunity to vaccinia

Methods: In a case-control study, 67 breast cancer patients aged 30-70 years who received standard cytotoxic chemotherapy and were disease free at least 1 year, were matched by age, sex and number of smallpox vaccinations with healthy controls. Smallpox immunity markers were examined.

Results: Cases had significantly lower levels of vaccinia specific total IgG and IgG1 (ELISA U/ml) (84 vs. 130, $p=0.04$ and 37.6 vs. 23.4, $p=0.02$), vaccinia specific neutralizing antibodies (PRNT50) (14 vs. 22, $p=0.015$), vaccinia specific memory B cell ratio (%) (3.5 vs. 4.75, $p=0.0008$) and IFN γ levels (pg/ml) (25.4 vs. 104.4, $p=0.008$) as compared with the healthy controls.

Conclusions: Immunity to smallpox is reduced following cytotoxic chemotherapy treatment of breast cancer patients. This finding has to be considered if planning a smallpox vaccination campaign. The effect of immunosuppressive treatments on persistence of immunity should be tested in relation to other vaccines given along the life span.

H. PYLORI SERO-POSITIVITY IS ASSOCIATED WITH LOW SERUM FERRITIN LEVELS IN ISRAELI ARAB CHILDREN –A SERO-EPIDEMIOLOGICAL STUDY

Muhsen K. ^{1,2}, Barak M. ³, Nir A. ¹, Shifnaidel L. ³, Bassal R. ², Cohen D. ^{1,2}

¹ Department of Epidemiology and Preventive Medicine, School of Public Health, Sackler Faculty of Medicine – Tel Aviv University, Tel Aviv, Israel

² Israel Center for Disease Control, Ministry of Health, Gertner Institute Tel Hashomer, Israel and ³ Clalit –Health Services, Haifa and Western Galilee Laboratories, Haifa, Israel

Background: The possible contribution of *H. pylori* infection to iron deficiency has been recently assessed but the results are still controversial.

Objectives: To examine the association between *H. pylori* and low serum ferritin levels during childhood, in a population with high prevalences of both anemia and *H. pylori* infection.

Methods: We carried out a sero-epidemiologic study using sera of 509 Israeli Arab children aged 1-19 years. Serum ferritin levels were measured using the immuno-turbidity assay and the presence of specific IgG antibodies to *H.pylori* was detected by ELISA. ELISA was also used to measure sero-positivity to *H.pylori* CagA.

Results: The *H. pylori* sero-positivity was 47.3%. A low ferritin level was found among 58 (11.4%) of the participants. A higher prevalence of low ferritin levels was observed among *H. pylori* sero-positive participants as compared with *H. pylori* sero-negative subjects; 14.5% and 8.6% respectively; prevalence ratio 1.7, (95% CI: 1.03-2.8) (p= 0.035). There was a dose response relationship between the prevalence of low ferritin and *H. pylori* IgG levels in the serum. A trend for a higher prevalence of low ferritin levels was detected among *H. pylori*-CagA sero-positive children.

The multi-variate analysis revealed a 4.7-fold increased risk for low ferritin level only among children aged ≤ 5 years, after controlling for sex and socioeconomic status: adjusted OR 4.7 (95% CI: 1.6-13.9) p=0.005.

Conclusions: In a pediatric population with high rates of both *H. pylori* infection and anemia, infection with *H. pylori* is associated with an increased risk for low ferritin levels, with young children being at the highest risk.

APPLICATION OF KNOWLEDGE DISCOVERY IN DATABASES (KDD) TO DEFINE THE INFLUENCE OF METHICILLIN RESISTANCE ON THE MORTALITY OF PATIENTS WITH NOSOCOMIAL *S. AUREUS* BACTEREMIA

Ziv T.¹, Leshno M.^{2,3}, Maor Y.^{1,3}, Cohen D.¹, Keller N.⁴, Rotstein Z.^{1,3,4}, Rahav G.^{2,4}

¹Department of Epidemiology and Preventive Medicine, School of Public Health, ²Sackler Faculty of Medicine, ³Faculty of Management, Tel Aviv University, ⁴Sheba Medical Center.

Background: *S. aureus* bacteremia is associated with mortality rates of 20%-50%. Infections caused by resistant organisms are associated with increased mortality. Studies comparing outcomes in MSSA/ MRSA bacteremia found conflicting results.

Objectives: To identify a subgroup of patients with nosocomial *S.aureus* bacteremia in whom MR influenced on the mortality.

Methods: A retrospective population-based cohort study of all patients hospitalized in Sheba Medical Center, a 1480-bed tertiary university hospital in Israel. All nosocomial SAB during 2005 were included in the study (n=141). Hospital computerized databases were used. Chi-squared Automatic Interaction Detector (CHAID) and Classification and Regression Tree (CRT) were used to identify risk factors for in hospital mortality, and were compared to multivariate logistic regression (MLR).

Results: MLR demonstrated that MR was not associated with mortality. Multivariate CHAID and CRT revealed that renal failure (RF) was the most influential factor on mortality (52.1% and 23.7% respectively, p=0.002). In patients with RF, diseases of blood and blood forming organs (DBF) were the best predictors for mortality (45.2% in those with 0 or 1 DBF and 100% in those with >1 DBF, p=0.024). Only those patients with RF and with 0 or 1 DBF were influenced by MR (25.0% and 63.6% mortality among MSSA and MRSA; p=0.012). The relative risk for mortality among this subgroup was 2.55 (p=0.012) compared to 1.36 (p=0.34) in all other patients.

Conclusion: CHAID and CRT revealed that only in those patients who suffered from renal failure and 0 or 1 DBF, MR was associated with increased mortality.

TICK-BORNE ENCEPHALITIS – EPIDEMIOLOGY AND VACCINE PREVENTION

*Rendi-Wagner, Pamela*¹

¹ Department of Epidemiology and Preventive Medicine, School of Public Health, Sackler Faculty of Medicine, Tel Aviv University, Israel and Department of Specific Prophylaxis & Tropical Medicine, Medical University Vienna, Austria

Tick-borne encephalitis (TBE) poses a significant public health problem in Scandinavia, western and central Europe, Russia, as well as some parts of northern Asia. During the last decades TBE incidence rates have increased temporally as well as spatially in several endemic countries apart from Austria, where an extensive national vaccination program is in place. With no specific treatment, TBE poses one of the most serious vector-borne infections of humans. Transmission to humans usually occurs via the bite of an infected tick (*Ixodes ricinus* or *Ixodes persulcatus*) and more rarely following consumption of infected unpasteurized dairy products. Risk of TBE infection depends mostly on season and degree of outdoor exposure to forested areas. On the basis of excellent epidemiological data available in Austria, a considerable risk of TBE disease of 1:10,000 per man-month of exposure may be estimated. Yet, active immunization appears to be the most effective tool of TBE prevention. Although a number of TBE vaccines are in current use, not all of them have been subject to rigorous placebo-controlled, comparative efficacy trials. In Central and Western Europe, TBE vaccines are marketed by two manufacturers. Long-term experience gained from widespread use, however, prompted the development of improved vaccine formulations of the two licensed European TBE vaccines. Moreover, recent clinical trials also suggested maintenance of high values of post-vaccination neutralizing TBE antibodies for a period longer than expected, thus also resulting in modifications with regard to immunization regimens. Recent advances in recombinant DNA technology have opened future opportunities for developing novel live attenuated vaccines against TBE virus and other flaviviruses.

GROUP B STREPTOCOCCAL CARRIAGE IN JEWISH AND ARAB PREGNANT WOMEN IN NORTHERN ISRAEL – PREVALENCE AND RISK FACTORS

*Ephros , M.*¹

¹Department of Pediatrics, Carmel Medical Center, and the Faculty of Medicine, Technion, Haifa, Israel

Background: From a number of small focal studies, the Israeli incidence of invasive early onset Group B streptococcal (GBS) disease is low. In addition, a higher attack rate amongst Jewish infants but a higher mortality among Arab infants was noted, primarily in northern Israel. Given a number of recent local studies showing increased GBS carriage, given the possibility that increased carriage might be associated with more disease, it is important to assess current GBS carriage rates among Jewish and Arab pregnant women, particularly in northern Israel, as well as the risk factors associated with carriage in both groups, aiming to further understand the differences noted between Jews and Arabs, and to assist in determining the most suitable neonatal GBS preventive policy in Israel.

Objectives: To evaluate the prevalence and the risk factors for GBS carriage among Jewish and Arab pregnant women, as well as the GBS serotypes among women in northern Israel.

Methods: In a cross-sectional study 732 Jewish and Arab pregnant women (Jews 57%, Arabs 43%) ≥ 35 weeks pregnant, from 3 hospitals in northern Israel were examined. Information regarding risk factors for GBS carriage was obtained from questionnaires filled out by participants in the study. GBS carriage was documented by swabbing the lower vagina and rectum and growing GBS on selective broth medium. Confirmation was by agglutination with specific antiserum. Identification of serotypes was by the Lancefield method. Additional GBS isolates from vaginal swabs obtained from pregnant women in the same hospitals but not in the study were also serotyped. Prevalence rates with 95% confidence interval were calculated for GBS carriage in both sectors. To examine the association between various risk factors and GBS carriage rate univariate analysis was performed for the general study population and among the Jewish and Arab subgroups. For

each variable an odds ratio, as an estimate for relative risk, with a 95% confidence interval was calculated. Chi-square test and Fisher's exact test for small sample sizes were used to determine statistical significance of differences in GBS carriage rates between the various groups. The variables that were found to be significantly associated with GBS carriage in the univariate analysis were further tested in multivariate analysis models using logistic regression. In addition, the distribution of the different GBS serotypes was evaluated.

Results: The prevalence of GBS among the general study population was 14.3%, and among the Arab and Jewish subgroups prevalences were 17.8% and 11.7%, respectively ($p=0.02$). In the univariate analysis among the general study population, low income level and fewer years of education were found to be statistically associated with higher carriage rates, whereas past abortion was associated with lower carriage rates. No significant associations for GBS carriage were found in the Arab sector. In the Jewish subgroup however, young age, low income level and birth country other than Israel (especially former USSR) were significantly associated with higher carriage rates, whereas past abortion was associated with lower carriage rates. In the multivariate analysis carried out among the general study population, there was a significant association between higher carriage rate and low income as well as less education. In the Jewish subgroup 2 possible models were tested, and in both, lower income and birth country were found to be significantly associated with higher carriage rates. Serotype distribution among GBS-positive women in the general population was: B untypable (8%), Ia (17%), II (23%), III (22%), V(12%), others (28%). No significant differences were noted between Jewish and Arab women's serotypes.

Conclusions: Arab pregnant women had a higher GBS carriage rate than Jewish pregnant women. In the Jewish sector, an income level per house of ≤ 6000 NIS per month and less education were significant risk factors for higher GBS carriage. The dominant serotypes in the general population were serotypes Ia, II and III. Due to increasing GBS carriage in northern Israel, and in agreement with other Israeli data (e.g. Jerusalem, Beer Sheva, Nahariya) the existing national policy should be reevaluated, however this must be done primarily in the context of the incidence of early onset invasive GBS disease.

היארעות מחלה פולשנית מוקדמת הקשורה ל- *Streptococcus gr. B* בילודים, בשנים 2006-2007 בישראל

מיכל ברומברג¹, עדי ליבלינג¹, תמר שוחט^{1,2}

¹ המרכז הארצי לבקרת מחלות, משרד הבריאות; ² החוג לאפידמיולוגיה ורפואה מונעת, אוניברסיטת תל אביב

רקע: מינהל רפואה קבע ביולי 2005 כי אין מקום לבצע בדיקת סקר לנוכחות חיידק הסטרפטוקוקוס מקבוצה B (GBS) בנשים הרות באופן שגרתי, אלא בנשים הרות עם גורמי סיכון מוגדרים. בשנים האחרונות נצפתה עלייה בשיעורי הנשאות של GBS בנשים הרות באזורים שונים בארץ.

מטרות: לאמוד את שיעורי ההיארעות של invasive GBS (iGBS) בשבוע הראשון לחיים בשנים 2006-2007 בישראל.

שיטות: מחלקות הילודים והמטבדות הבקטריוולוגיות ב-23 ביה"ח הכלליים בארץ התבקשו לדווח על מספרי הילודים שחלו ב-iGBS בשבוע הראשון לחייהם במוסדיהם על פי שנת תחלואה, לאום, והשתייכות האם לקבוצת סיכון. חושבו שיעורי היארעות של iGBS עבור כל שנה בנפרד וממוצע דו שנתי, כל ביה"ח בנפרד וכלל ביה"ח, וילודים שנולדו לאימהות שהינן ושאינן בקבוצת הסיכון המוגדרות (הנחנו כי 20% מכלל הנשים ההרות נכללות בקבוצת הסיכון).

תוצאות: התקבלו דיווחים מ-22 ומ-21 ביה"ח עבור 2007 ו-2006, בהתאמה. סה"כ דווח על 94 מקרי תחלואה (47 בכל שנה). מתוכם ל-80 ידוע שיוך לקבוצת סיכון. שיעור ההיארעות הגולמי הממוצע של iGBS בשבוע הראשון לחיים ב-2006-2007 בישראל הינו 0.35 ל-1,000 לידות חי (95%CI 0.29-0.43). שיעור ההיארעות בילודים שאמהותיהם משתייכות לקבוצת הסיכון הינו: 0.75 ל-1,000 לידות חי (95% CI 0.54-1.05), לעומת 0.25 ל-1,000 לידות חי (95% CI 0.19-0.34) בקרב ילודים שאמהותיהם אינן בקבוצת הסיכון. במרבית ביה"ח בארץ שיעורי התחלואה הגולמיים ב-iGBS אינם עולים על 0.5 ל-1,000 לידות חי, הסף שנקבע לצורך ביצוע בדיקות סקר לנשאות בנשים הרות באופן שגרתי. בביה"ח בהם נצפתה חריגה מהסף הנ"ל, על פי רוב, היא לא הייתה עקבית במהלך השנתיים שנבדקו. שיעורי התחלואה בילודים ללא גורמי סיכון אימהיים היו נמוכים יותר מהשיעורים הגולמיים. שיעורי תחלואה גבוהים נצפו בקרב ילודים עם גורמי סיכון אימהיים.

סיכום: לדעתנו, אין כיום צורך בשינוי המדיניות הקיימת, לפיה יש לסקור רק את הנשים ההרות הנמצאות בקבוצת הסיכון שהוגדרו. יש להמשיך ולעקוב אחר שיעורי ההיארעות לפי קבוצות הסיכון ולהעריך תקופתית אם יש צורך בשינוי הנוהל הקיים. כמו גם לבחון את הסיבתיות להיארעות הגבוהה יחסית שנצפתה בילודים המשתייכים לקבוצת הסיכון.

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Secound Session

Chairman: Dr. Moshe Ephros (Efrat), Carmel Medical Center & Technion

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Dr. Pamela Rendi-Wagner

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**The meeting will be held at "Lola" hall, Sackler Faculty of Medicine,
Tel Aviv University Campus**

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פורום מחקר באפידמיולוגיה של מחלות זיהומיות וביטחון ביולוגי

תוכנית מפגש מס' 1

10/7/2008

13:00 התכנסות, הרשמה וכיבוד קל

13:30 דברי פתיחה

פרופ' יוסי מקורי

דיקאן הפקולטה לרפואה ע"ש סאקלר

פרופ' מרדכי שני

ראש בית הספר לבריאות הציבור

פרופ' דניאל כהן

ראש החוג לאפידמיולוגיה ורפואה מונעת ומנהל המרכז לחקר טרור ביולוגי

מושב ראשון

יו"ר פרופ' תמר שוחט – המרכז הלאומי לבקרת מחלות ואוניברסיטת תל אביב

14:00 אפידמיולוגיה מולקולרית וסרו-אפידמיולוגיה של *Vibrio vulnificus*, בישראל

ד"ר נאיל בישראל

מרכז רפואי העמק והחוג לאפידמיולוגיה ורפואה מונעת, אוניברסיטת תל אביב

14:30 השפעת טיפולים מדכאי חיסון על חסינות ארוכת טווח לאבעבועות שחורות

ד"ר איתי וייזר

החוג לאפידמיולוגיה ורפואה מונעת, אוניברסיטת תל אביב

15:00 הקשר בין זיהום ב-*Helicobacter pylori* ומשק ברזל נמוך בקרב ילדים ערבים בישראל

גב' ח'יתאם מוחסן

החוג לאפידמיולוגיה ורפואה מונעת, אוניברסיטת תל אביב

15:30 יישום שיטות לגילוי ידע להשוואת תמותה בחולים עם אלח דם נוזקומיאלי

מ-*Staphylococcus aureus* עמיד לעומת רגיש למתיצילין

מר תומר זיר

המרכז לחקר טרור ביולוגי והחוג לאפידמיולוגיה ורפואה מונעת, אוניברסיטת תל אביב

16:00 הפסקה

החוג לאפידמיולוגיה ורפואה מונעת והמרכז לחקר טרור ביולוגי

בית הספר לבריאות הציבור

הפקולטה לרפואה ע"ש סאקלר, אוניברסיטת תל אביב

קריית האוניברסיטה, רמת אביב

ת.ד. 39040, תל אביב 69978

טל': 03-6408572, פקס: 03-6409868

פורום מחקר באפידמיולוגיה של מחלות זיהומיות וביטחון ביולוגי

מושב שני

יו"ר ד"ר משה אפרת – מרכז רפואי כרמל והטכניון

Epidemiology and vaccine-prevention of Tick-Borne Encephalitis 16:30

Dr. Pamela Rendi-Wagner

Dept of Spec. Prophylaxis & Trop. Med. Center of Physiology & Pathophysiology,
Medical University Vienna, and Dept of Epidemiology and Preventive Medicine, Tel
Aviv University.

17:00 היקף וגורמי סיכון של נשאות *Streptococcus gr. B* בנשים הרות מהמגזר היהודי והערבי

באזור צפון הארץ

ד"ר משה אפרת

המרכז הרפואי כרמל והטכניון, חיפה

17:30 היארעות מחלה פולשנית מוקדמת הקשורה ל- *Streptococcus gr. B* בילודים, בשנים

2006-2007 בישראל

ד"ר מיכל ברומברג

המרכז הלאומי לבקרת מחלות, תל השומר

17:45 מחקרים סרו-אפידמיולוגיים בישראל על מצב החסינות מפני מחלות הנמנעות על ידי

חיסונים. מה ניתן ללמוד מהם ?

פרופ' דניאל כהן

החוג לאפידמיולוגיה ורפואה מונעת, אוניברסיטת תל אביב

18:15 דברי סיכום

המפגש יתקיים באולם "לולה", הפקולטה לרפואה ע"ש סאקלר

קמפוס אוניברסיטת תל אביב

האירוע בחסות חברת :



פרטים נוספים באתר האינטרנט : <http://www.tau.ac.il/~taucsb>

החוג לאפידמיולוגיה ורפואה מונעת והמרכז לחקר טרור ביולוגי

בית הספר לבריאות הציבור

הפקולטה לרפואה ע"ש סאקלר, אוניברסיטת תל אביב

קריית האוניברסיטה, רמת אביב

ת.ד. 39040, תל אביב 69978

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