Borten, M. and E. A. Friedman (1978). “Duration of colposcopic changes associated with trichomonas vaginitis.” Obstet Gynecol **51**(1): 111-3.

> The possibility that an abnormal Papanicolaou smear of the uterine cervix may be associated with vaginitis due to trichomonas vaginalis has been known for some time. Since colposcopy is being used with increased frequency to evaluate patients with cytologic abnormalities noted on the cervical smear and the colposcopic changes produced by trichomonal vaginitis are quite typical, a study was designed to evaluate the duration of these changes after effective eradication of the parasite. Among 12 patients in whom the infection was successfully treated, none showed evidence of colposcopically detected abnormalities due to the trichomonal vaginitis at 2 weeks and again at 4 weeks after initiation of therapy.

Gram, I. T., M. Macaluso, et al. (1992). “Trichomonas vaginalis (TV) and human papillomavirus (HPV) infection and the incidence of cervical intraepithelial neoplasia (CIN) grade III.” Cancer Causes Control **3**(3): 231-6.

> The temporal relationship between cervical infection with Trichomonas vaginalis (TV) or human papillomavirus (HPV) and the incidence rate of cervical intraepithelial neoplasia grade three (CIN III) was examined in a cohort of 43,016 Norwegian women. From 1980 to 1989, a cervico-vaginal infection from TV and HPV was diagnosed cytologically in 988 and 678 women, respectively. During the 181,240 person-years of observation, 440 cases of CIN III/cervical cancer developed. The age-adjusted incidence rates (IR) of CIN III were 225 per 100,000 person-years among women with no cytologic evidence of infection, 459 among women with TV infection, and 729 among women with HPV infection. A multiple regression model yielded a relative rate (RR) of CIN III of 2.1 (95 percent confidence interval [CI] = 1.3-3.4) among women with TV infection and 3.5 (CI = 1.9-6.6) among women with HPV infection, compared with women with neither infection. As CIN can be misclassified as HPV infection, the entry Pap-smears of 10 women with HPV infection who later developed CIN III were re-examined. Excluding the four discordant cases with the corresponding person-years decreased the RR of CIN III to 2.1 (CI = 0.9-4.8). Our report demonstrates the limitations of studies that rely only on cytologic detection of HPV infection. Nevertheless, the results support the hypothesis that HPV is a causal factor for CIN III lesions, and also display an association between TV infection and cervical neoplasia.

Mekki, F. and J. Ivic (1979). “[Significance of variations in the size of Trichomonas vaginalis in patients with dysplasia, intrapithelial and invasive planocellular carcinoma of the uterine cervix].” Jugosl Ginekol Opstet **18**(1): 15-9.

> The study of the size of Trichomonas vaginalis in 100 patients with dysplasia and intraepithelial or invasive planocellular carcinoma of the uterine cervix and in 100 controls with trichomoniasis alone has shown that the parasites are of a significantly smaller diameter in carcinoma in situ (9.57 +/- 0.35 mu) and invasive carcinoma (10.44 +/- 0.66 mu) than in dysplasia (13.71 +/- 0.35 mu). The analysis of the variance has shown that this difference is statistically significant. In the control group with trichomoniasis alone, the diameter of Trichomonas vaginalis was twice as large (21.46 +/- 0.66 mu) as that in carcinoma and still larger than that in dysplasia. This indicates that small forms of Trichomonas vaginalis are more pathogenic than large ones and might be one of the causative agents of the atypical transformation of the squamous epithelium of the uterine cervix.

Viikki, M., E. Pukkala, et al. (2000). “Gynaecological infections as risk determinants of subsequent cervical neoplasia.” Acta Oncol **39**(1): 71-5.

> A longitudinal cohort study was carried out to determine whether gynaecological infections other than human papillomavirus (HPV) are also related to the subsequent increased risk of cervical neoplasia. The study comprised 19114 women attending the organized mass screening in Finland in 1985-1990 with cytologically detected HPV, Actinomyces, herpes simplex, Trichomonas vaginalis, or yeast. The women were followed-up for subsequent preinvasive lesions and invasive cancers until the end of 1994 by linkage to the nation-wide Cancer Registry. Standardized incidence ratios (SIR) with rates for the whole of Finland as reference and 95% confidence intervals (CI) were estimated. Trichomonas vaginalis and HPV were associated with a high relative risk of cervical cancer, SIR 6.4 (CI 3.7-10, preinvasive lesion and invasive cancer combined) and SIR 5.5 (CI 4.2 7.2, preinvasive lesion and invasive cancer combined), respectively. Herpes simplex was rarely detected, but the highest and statistically most significant point estimate was observed (SIR 12, CI 2.4-34, preinvasive lesion and invasive cancer combined). Neither Actinomyces nor yeast was associated with a significantly increased risk of cervical cancer. None of these results could be accounted for by the confounding effect of the other infections. Our results, based on a prospective design, lead us to propose that Trichomonas vaginalis and herpes simplex virus are also predictors for cervical neoplasia.

Yap, E. H., T. H. Ho, et al. (1995). “Serum antibodies to Trichomonas vaginalis in invasive cervical cancer patients.” Genitourin Med **71**(6): 402-4.

> OBJECTIVE--To evaluate, by seroepidemiology, the possible role of the sexually-transmitted flagellate, Trichomonas vaginalis, in invasive cervical cancer. SUBJECTS AND METHOD--Sera from 121 invasive cervical cancer patients and 242 random age-matched female controls. Antibodies to T. vaginalis were detected by the western blot technique. RESULTS--Antibodies to T. vaginalis were detected in the sera of 41.3% (50/121) of invasive cervical cancer patients compared with only 5.0% (12/242) of female controls. All the reactive sera reacted strongly with the immunogenic surface membrane proteins of T. vaginalis of molecular weights of about 92 and 115 kDa, with variable reactivity to other immunogenic proteins of T. vaginalis. CONCLUSION--The significantly increased relative risk, RR = 3.42 (95% CI = 1.73-6.78), is comparable to the RRs derived in seroepidemiological studies of human papillomavirus, suggesting that T. vaginalis may be even more closely associated with invasive cervical cancer than previously realized.

Zhang, Z. F. and C. B. Begg (1994). “Is Trichomonas vaginalis a cause of cervical neoplasia? Results from a combined analysis of 24 studies.” Int J Epidemiol **23**(4): 682-90.

> BACKGROUND. We conducted this combined analysis of available data from studies with information on this issue to clarify the association between Trichomonas vaginalis infection and cervical neoplasia. METHODS. We performed MEDLINE searches (1966-1993) using the key words and phrases 'trichomonas vaginitis' and 'neoplasms, cervix' for articles published in English, and searched citations of the articles obtained from MEDLINE. A total of 24 articles (two cohort studies and 22 case-control) were included in this data analysis. In the analysis, the studies were evaluated for heterogeneity using Breslow-Day tests for homogeneity of the odds ratios and of rate

ratios. If the odds ratios from studies are heterogeneous, it is not appropriate to combine them using the Mantel-Haenszel method. Also, publication bias was evaluated by assessing the association between the observed effect size and the variance of the effect size using a rank correlation test. RESULTS. The combined summary relative risk for the two cohort studies was 1.93 (95% confidence interval: 1.22-2.65) indicating an approximate doubling of the risk of cervical neoplasia in the presence of T. vaginalis infection. The attributable risks among exposed subjects and among the source population were 47.4% and 2.1% respectively. Results of the 22 retrospective studies were much less consistent. However, most of them demonstrated a significant positive association. CONCLUSIONS. This combined analysis suggests that there is an association between T. vaginalis and the risk of cervical neoplasia, but that such infections account for only 2% of cervical neoplasia.

Zhang, Z. F., S. Graham, et al. (1995). "Trichomonas vaginalis and cervical cancer. A prospective study in China." Ann Epidemiol **5**(4): 325-32.

The relationship between Trichomonas vaginalis infection and cervical cancer was investigated prospectively in a cohort of 16,797 women aged 25 years or more who were followed from 1974 to 1985 within the framework of a cervical screening program in Jingan, China. Personal interviews were conducted by trained interviewers when the women first entered the screening program. At initial screening, 421 (2.51%) women had a positive cytologic diagnosis of T. vaginalis infection. Ninety-nine incident cases of pathologically confirmed squamous cell carcinoma were identified from the cohort, with a total of 140,018 person-years of observation. T. vaginalis infection was found to contribute to the risk of cervical cancer, as determined by crude estimates and after adjustment for potential confounding effects. In a multiple proportional hazards model, the relative risk for cervical cancer was 3.3 (95% confidence interval: 1.5 to 7.4) among women with T. vaginalis infection. Furthermore, in the multivariate analysis, increased risk of cervical cancer was associated with the following factors: number of extramarital sexual partners of both the subjects and their spouses, cigarette smoking, and irregular menstruation. Having a large number of negative Pap smears was associated with lower risk. This study suggests that there might be an association between T. vaginalis infection and the risk of cervical cancer, but only 4 to 5% of cervical cancer in Chinese women may be attributable to T. vaginalis infection.