14. Risk factors for gallstone disease: genetic, ethnic and environmental factors

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Gallstones are a major public health problem in all developed countries. Available evidence suggests that the incidence of gallstones has been rising sharply in recent decades [1, 2]. Like many chronic, non infectious diseases whose incidence increases with age, the pathogenesis of gallstones may be multifactorial. Much has been learned in recent years about factors in bile associated with cholesterol gallstone formation; however the reasons for the rising incidence of gallstones remain unknown. There is evidence to support the existence of all 3 factors which are the subject of the present discussion.

The presence of genetic factors is suggested by the increased familial prevalence of gallstones which has been found in ethnically homogeneous populations living under similar environmental conditions. Surprisingly few studies have been performed on familial factors in gallstone disease and even fewer studies where asymptomatic first degree relatives were investigated. Our study was initiated to assess the prevalence of gallstones in family members of patients with proven gallstones versus a matched control group [3].

A tremendous ethnic variation has been demonstrated in the prevalence of gallstones in studies conducted in various parts of the worlds including in our area, as shown by the considerable differences in the prevalence of gallstones between Jews in Tel Aviv and Arabs in Gaza [4, 5]. In many of these cases it is difficult to disentangle between environmental and ethnic — genetic factors. We chose to study two populations, Jews in Tel Aviv and Arabs in Gaza, who share some genetic traits (like lactase deficiency) as well as geographic and climatic conditions. The main differences were dietary and cultural habits. The purpose of this study was to compare the composition of the diet of these two populations.

Family study

In the early 80's we performed a study of 175 first degree relatives of patients (101 women, 66 men) with proven gallstones versus 200 (87

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women, 113 men) matched controls. First a patient with gallstones (pro­
positus) proven by X-ray, operation or autopsy was identified. Only if he had
at least one first degree relative (parents, siblings or children above age 20)
was his family included in the study. Almost all were asymptomatic. For each
family member examined a control subject were sought and similarly exam­
ined. The controls were staff members of the hospital and clinic patients with
minor diseases mostly from the dermatologic and ophtalmologic outpatient
clinics. We tried to match the control group with the family group by sex, age
and community group.

An oral cholecystogram was performed after an overnight fast following
the ingestion of 500 mg of iopanoic acid per 20 kg body wt 14 hr before the
X-ray examination. In cases of nonvisualization of the gallbladder, the study
was repeated using a double dose and if there was again no opacification, an
intravenous cholangiogram was performed.

Ultrasound was not widely available at the start of the study.

Results

Gallstones were found in 20.5% of the family group and in 9% of the control
group (Fig. 1). The differences were statistically significant for the whole
group as well as for women and men separately ($P < 0.01$). Because age,
sex, weight and ethnic origin are very important risk factors, the frequency of
gallstones in each of these groups was compared separately (Figs. 2—4). The

![PERCENT WITH STONES](image)

*Fig. 1.* Frequency of gallstones in family and control groups.