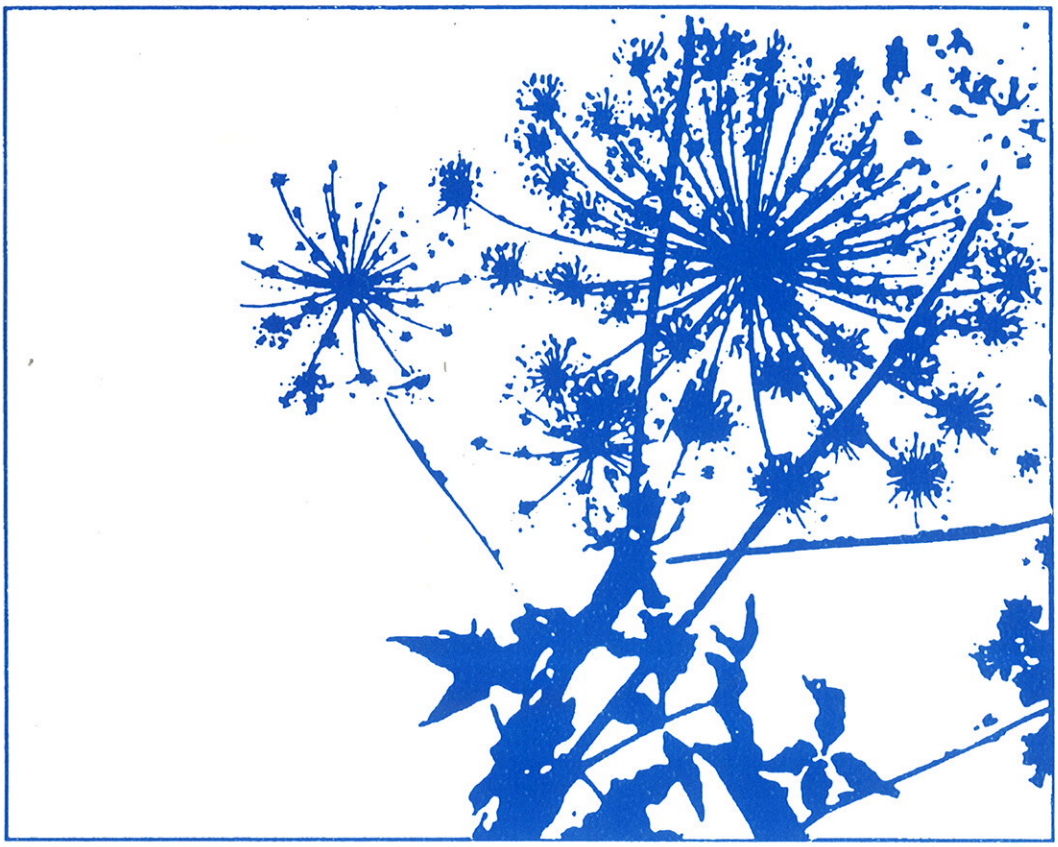
ISM skriftserie Nr. 37



THE SØRREISA GASTROINTESTINAL DISORDER STUDY

Dyspepsia, peptic ulcer and endoscopic findings in a population.

Bjørn Bernersen

**Institute of Community Medicine,
and Institute of Clinical Medicine,
University of Tromsø**

ISM skriftserie
blir utgitt av Institutt for samfunnsmedisin
Universitetet i Tromsø.

Forfatterne er selv ansvarlige for sine funn og konklusjoner. Innholdet er derfor ikke uttrykk for ISM´s syn.

The opinions expressed in this publication are those of the authors and do not necessarily reflect the official policy of the institutions supporting this research.

ISBN 82 – 90262 – 43 – 4
1996

Public relation: Mayor of Sørreisa Kjell A. Bakkland and the author.

Contents page

ABSTRACT

The Sørreisa Gastrointestinal Disorder Study was conducted in 1987 as a collaborative work between The University of Tromsø, The University Hospital of Tromsø and the Primary Health Care Centre of Sørreisa.

The study was designed to study the prevalences of gastrointestinal symptoms, non-ulcer dyspepsia and of peptic ulcer in a general population. Further to investigate the relation between non-ulcer dyspepsia and peptic ulcer by their distribution in this general population and their associations to lifestyle and psychological factors, and to explore the occurrence of endoscopic, microbiological and histological findings and their associations to dyspeptic symptoms.

The study comprised a survey by a postal questionnaire with 119 questions on abdominal complaints, health, life-style, diet and social conditions sent to all inhabitants 20 to 69 years old. A clinical investigation of all dyspeptics and of matched controls, including an upper endoscopy and blood sampling, was done. All medical records in the Primary Health Care Centre were searched for confirmation of a peptic ulcer diagnosis and if the subjects had consulted for dyspeptic problems.

The questionnaire response rate was 88.9% among 2027 men and women. Subjects ever having upper abdominal pain for at

least two weeks and/or heartburn or acid regurgitation almost daily for at least one week's duration were considered having dyspepsia. Of 495 subjects having dyspepsia, 137 were excluded, leaving 362 subjects, of whom 309 together with 310 controls were endoscoped (79.2 % of all subjects invited) in a blinded procedure.

Men reported dyspepsia (30.4%) and peptic ulcer (8.7%) more often than women (24.1 and 5.2 %, respectively). Peptic ulcer had an overall prevalence of 10.5 % in men and 9.5 % in women and a higher duodenal/gastric ulcer ratio than reported earlier in northern Norway and the earlier opinion on sex ratio for peptic ulcer is questioned. Asymptomatic subjects had peptic ulcer in 1%. Non-ulcer dyspepsia was frequent in both genders and age groups up to 60 years, with a marked decrease above this age. Non-ulcer dyspepsia was associated with having a family history of peptic ulcer and dyspepsia and the use of tranquillizers. Dyspepsia is common, but seldom associated with peptic ulcer up to the age of 40 years.

Only 10-15 % of both dyspeptic and asymptomatic subjects had a histologically normal mucosa. Only peptic ulcer disease, endoscopic duodenitis and histologically confirmed active chronic gastritis were found more often in dyspeptic than in asymptomatic subjects. Helicobacter pylori positive cultures from gastric mucosa were found in 48 % of dyspeptic subjects

and in 36% of asymptomatic subjects. Positive Helicobacter pylori cultures were associated with gastritis and peptic ulcer. Pathological findings in the duodenal and gastric mucosa are frequent and there is with few exceptions, a lack of association with dyspepsia.

The findings challenges gastroenterologists and pathologists to search for new distinctions between disease and non-disease. The epidemiological approaches are mandatorial when new diseases are identified or new technology is introduced as a routine among our armamentaria.

ACKNOWLEDGEMENTS

I am grateful to my superior and friend professor Per G. Burhol who, with all his skills and experience, must have known what he did, what I did not, when he led me into the first steps of scientific work. I am still awaiting his story: «How to recruit research fellows against every odds".

I am constantly aware of my luck and am grateful for the fortunate meeting with people from the Institute of Community Medicine in Tromsø, where I could overcome a somewhat difficult position as an elderly novice, due to a respectful treatment and adequate education. The open doors at the Institute gave me access to several high quality researchers who gave me practical help with many items. I must mention professor Egil Arnesen, professor Olav Helge Førde, The late secretary Gunn Eva Andersen, assistant professor Tormod Brenn and Gunnar Ellingsen.

Primus inter pares was my colleague and friend professor Roar Johnsen, now just primus, but still the indispensable guide, inspirator, teacher and discussion partner through my work with the Sørreisa GID study.

Associate professor Bjørn Straume has been my co-worker and teacher, managing to combine these tasks and still being my friend, comforting me with excellent home-made food, beverages and long-standing conversations.

The nurses Selma Eri Finnseth, Lise Gulbrandsen and Martha Øvermo, were my good helpers and companions in Sørreisa, who, besides doing skilled work, helped to keep a high spirit and to give me lessons on Sørreisa.

Torhild and Per A. Stakkevold were interested inspirators, held an open house with all facilities for me, and helped me in many practical matters.

Vigdis Brox Pettersen had the unpleasant task to receive my Helicobacter pylori tubes at any time and to keep them warm, She smiled every time. Besides she made a professional work on this material in the microbiological laboratorium.

Smith Kline & French and Searle Norge supported our study financially. I especially thank Kari Hafenbrädl of Searle Norge for her great practical help.

Polack Norge A/S provided me with a fully equipped endoscopic laboratory and has never sent me the bill.

The Norwegian Council for Science and Humanities granted me a scholarship for two years as a clinical research fellow.

PREFACE

Personal background.

I had been a clinician and gastroenterologist for years and years, and concentrating on patient problems and specific clinical topics, I had forgotten what medicine else could be. I had forgotten to look outside the hospital, and small glimpses of the outer world were soon forgotten in this absorbing environment.

During a short stay at the University Hospital in Tromsø in 1986, I was confronted with a new upcoming idea of a scientific work about non-ulcer dyspepsia. The exciting idea was to find the patients with dyspepsia before deciding to see their doctor and to relate their dyspepsia to environmental and clinical findings. I found it very interesting and accepted to be a co-worker. After some time I found myself working only together with professor Per G. Burhol on these plans and was soon thereafter the leader of a small team. During several meetings with people from the outer world, foremost epidemiologists, I began to realise that many aspects, not inherent in daily clinical work, had to be considered.

Introduction to scientific work (The scientific story).

Non-ulcer dyspepsia was becoming a very popular topic and we followed the development of scientific work in this field. We found the work of Olof Nyrén from the Uppsala county most impressive and this work nourished our idea of going to the very bottom of our source of patients (1). Dr. Nyrén had investigated dyspepsia patients from the Uppsala county during two years and had used population controls in a case control study. He concluded that non-ulcer dyspepsia was not significantly associated with organic diseases and that the condition might be a disease entity with a different pathophysiological mechanisms from duodenal ulcer, and psychological factors might be crucial in the aetiology. From his case-control study he concluded that acid reduction therapy was without beneficial effect in non-ulcer dyspepsia (2). We were curious to relate non-ulcer dyspepsia to other possible pathogenetic factors and especially to see if non-ulcer dyspepsia was related to life-style and social factors.

1. INTRODUCTION

Somebody in your nearest surroundings will have digestive disorders if you do not have these problems yourself. People will try to describe their digestion problems with words or other expressions varying in time and cultural settings and doctors have used much fantasy to interpret them. The aetiology of symptoms is unclear. Symptoms have a great variability and despite attempts to understand digestive symptoms and to classify them on the background of culture and environmental conditions, on pathogenesis or aetiology, these attempts have not been entirely satisfying (3). Authors agree that dyspeptic symptoms are common (4,5) but it is difficult to define exactly what dyspeptic symptoms are (6). Besides, having tried to define special groups of dyspepsia, many authors temporarily used terms, like x-ray negative dyspepsia (7) and pseudo-ulcer syndrome(8) and more actual definitions like non-ulcer dyspepsia and epigastric distress syndrome (1). We have lately made little progress in understanding dyspepsia and relating the symptoms to disease(9) and the natural course of dyspepsia is known only to a modest extent. Scientific interest in dyspepsia has in our near past mainly been concentrated upon the relation to peptic ulcer and other changes in the mucosa seen endoscopically or microscopically

(10,11). The diagnostic methods have been limited and diagnoses have relied upon techniques mostly available in hospitals or specialist centres. General practitioners have selected patients for diagnostic procedures with the idea that type and severity of dyspepsia would predict the important diagnoses (12-14).

Epidemiology.

Epidemiologists will look at the distribution of dyspeptic symptoms in a population to see if it can give an indication of the origin of symptoms, culturally, environmentally or genetically. Modern population based studies on dyspepsia stresses the high prevalence and also a high incidence and that dyspepsia consumes a great amount of health services (15,16).

The Pathogenetic viewpoint.

We have a long tradition of explaining dyspepsia pathogenetically on the basis of historical studies (17). Earlier this tradition was dominated by x-ray studies of motility and structure of the upper gastrointestinal tract. Lately we have got the endoscopic studies emphasising mucosal

pathology. We also had a long period of studies on gastrointestinal hormones and secretion studies, also concentrating on the functional putative pathophysiology of the upper gastrointestinal tract. And again we are moving into studies on motility by ultrasound techniques

Specific diagnoses:

Gastritis

Dyspeptic symptoms have in modern time in the opinion of doctors been related to peptic ulcer and gastritis (12) but also to functional disorders (6). Gastritis was for a long time used
synonymously with dyspepsia (16). The development of fiberoptic endoscopes with biopsy facilities have changed this diagnosis to a pathological anatomic diagnosis. Gastritis prevalences have been obtained in great population studies, showing that gastritis is common, increasing with age, but not associated with dyspeptic symptoms (18). New interest and progress in the understanding was stimulated by the rediscovery of curved bacteria in the stomach mucosa, now Helicobacter pylori (H. pylori) (19). The initial process of inflammation is associated with the occurrence of Helicobacter.

Peptic ulcer occurrence has varied with time and location and has been an enigma for clinicians and scientists. Diagnosis of peptic ulcer has evolved from merely using clinical observation to x-ray investigation and lastly endoscopic visualisation with possibilities for biopsies and histological verification or exclusion of malignancy. During the last 50 years, peptic ulcer has been found more frequently in men than in women in western countries. When subdividing peptic ulcers into gastric and duodenal ulcers this sex difference is found mainly to apply to duodenal ulcers, whereas gastric ulcers have been found about equally frequently in both genders. The scientific work on ulcer aetiology has mainly concentrated upon acid secretion and acid secretory related physiology and during the nineteenseventies great achievements in ulcer therapy took place (20). The rediscovery of spiral bacteria in the stomach mucosa in 1982 and the research on Helicobacter pylori, has turned research on peptic ulcer aetiology in a new direction and ulcer occurrence may also be better understood (21). There are, however, still some questions to ask. We do not know the natural course of Helicobacter pylori (H. pylori) infection

and we do not know the long term effect of H.pylori eradication.

"Localisation" of dyspepsia

Modern scientific studies and new methods have required subdivision of dyspeptic symptoms aiming at a better understanding of the nature of the symptoms(3). Many researchers have used hospital patients for their studies. This has made it difficult to agree on definitions of dyspepsia and to make comparisons between studies.

Several terms, which were aimed at explaining dyspepsia, have been introduced, like gastritis, duodenitis and gastro-oesophageal reflux without sufficient research to clarify if these terms were meaningful in an explanatorial or prognostic context.

In spite of much research, it is still unclear if the findings in the oesophageal, stomach or duodenal mucosa are associated with dyspeptic symptoms. It is also unclear how and to what extent dyspeptic symptoms or the finding of an ulcerous or inflamed mucosa in the upper gastrointestinal tract are associated with life-style, food habits, heredity, infectious disease and other environmental factors.

2. DESIGN OF THE SØRREISA GASTROINTESTINAL DISORDER STUDY.

2.1. The idea

When planning and conducting the study, we had the idea of going to the unselected population to elucidate the basis of selection for diagnostic procedures and treatment. We wanted to register persons having dyspeptic symptoms, to reveal prevalences of non-ulcer dyspepsia, irritable colon and peptic ulcer. We hoped to explore the associations between these entities and living conditions and lifestyle. Furthermore, we wanted to investigate the associations between dyspeptic symptoms and endoscopic findings. We also had the intention to collect a big sample of endoscopic duodenal biopsies and to describe the prevalence of the newly described bacterium Campylobacter (Helicobacter) pylori in dyspeptics.

2.2. The process

The first plans were drawn at the Laboratory of Gastroenterology at the Medical Department of the University Hospital in Tromsø. Several co-workers were involved with professor Per G. Burhol as leader. The group had several meetings where gastroenterologists discussed the items of this

project. We also had a general practitioner in the group Per A. Stakkevold. We had some few meetings with an experienced gastroenterologist and epidemiologist Olav Bonnevie and with an experienced local epidemiologist professor Dag S. Thelle. Later on we formed a smaller group with members from the Laboratory of gastroenterology and from the Department of Pathology at the University Hospital in Tromsø and members from the Institute of Community Medicine at the University of Tromsø. The members in this group were professor of gastroenterology Per G. Burhol, consultant pathologist Leif Bostad, research fellow in general practice Roar Johnsen, associate professor in epidemiology Bjørn Straume, general practitioner Per A. Stakkevold and myself as the leader.

2.3. The discussion

The discussions were mainly concentrated on a few topics: the questions in our questionnaire, the possibility of performing gastroscopy on healthy people, the possibilities of blinding on different levels and feasibility of the procedures performed in a local health centre.

The work with our questionnaire was an exhausting task. Firstly the discussion on characterising dyspepsia. Secondly lengthy discussions on possible risk factors, by dint of

searching in the literature and the use of strong fantasy. The first idea during this work was to evaluate the questionnaire and offer an upper endoscopy to all dyspeptics. Our experienced epidemiologists, however, convinced the group, after some discussions, of the absolute need of having healthy controls.

The third point was a discussion on how to perform an unbiased endoscopy procedure. Our resources of experts for endoscopy were one person, and we did not have the possibility to make video-taping of the endoscopies. This possibility was at hand only for a couple of days to record the routine of the procedure.

We chose a case-control setting to be able to evaluate whether our findings in dyspeptic subjects were directly related to their symptoms. Control subjects would be people without any experience of dyspepsia. We needed for this purpose a well defined population with minimal migration.

The Sørreisa community; why Sørreisa?

As a lucky coincidence we had, as mentioned above, the experienced general practitioner Per A. Stakkevold at the department. He told us about his work in the community of Sørreisa. This community had a stable population and health

service had been well functioning for a long period and seemed suited for our purpose, a population based study on dyspepsia and related diseases. The community had an appropriate size of the population with approximately 3500 inhabitants. The age and sex distribution similar to the distribution of the total Norwegian population. One fourth part of the population lived in a small township, the rest scattered over 361 square kilometres. The inhabitants were occupied in industry (Wood processing, metallurgical work, iron and metal work)(24 %), agriculture, forestry and fishing (4 %), construction work (10 %), trading, restaurant and hotel work (13 %) and in teaching, health service and administration (49 %).

The community had only one community health centre and the health services had been stable without vacancies of medical personal for years.

2.4. Ethical considerations

To expose healthy non-dyspeptic people to an unpleasant and potentially risky investigation was discussed thoroughly. Reported complications of gastroscopy and biopsy from the upper gastrointestinal tract in the hands of skilled endoscopists were very infrequent. From the Tromsø Heart Study and other surveys, we were aware of the general willingness of

people from Northern Norway to participate in scientific studies. We were convinced of the importance of having an open policy on the nature of our study. We also discussed the procedures to follow if any illness was found among our study subjects. We had open access to the local general practice and to the University Hospital in Tromsø. We did not discuss problems of medicalisation. With this background, we decided to apply for approval of the project by the Regional Committee for Medical Research Ethics and I met with the committee to explain our methods and our knowledge about complications. Our study and the different methods and procedures were accepted. All persons participating were insured against any damage related to the endoscopic or blood sampling procedure amounting to maximum one million Norwegian Kroner each.

2.5. The objectives of this study were

I. To study the prevalences of gastrointestinal symptoms, non-ulcer dyspepsia and of peptic ulcer in a general population.

II. To investigate the relation between non-ulcer dyspepsia and peptic ulcer by their distribution in this general population and their associations to lifestyle and psychological factors.

III. To explore the occurrence of endoscopic, microbiological and histological findings and their associations to dyspeptic symptoms.

2.6. The final design

Choice of methods

The study was based on three different elements. Firstly, a survey by a postal questionnaire distributed to all persons above 20 years. Secondly, to perform a clinical investigation of all dyspeptics and of matched controls, including an upper endoscopy and blood sampling. The third element was to investigate all local medical records to confirm peptic ulcer diagnoses, to record whether the subjects had consulted their doctor for dyspeptic problems and whether they had undergone diagnostic procedures.

We chose to conduct a study of adult people. We would start at the age of 20 as we could foresee several problems with the participation of younger people, foremost a low response rate. Later on, we decided to stop at the age of 70 years for the same reasons. We composed a comprehensive questionnaire where the questions partly were constructed for the aims of this study, partly were borrowed from other surveys, foremost the Tromsø Heart Study, where questions had been used and evaluated through several population studies. The questionnaire was tested on several healthy people and

some hospital patients to see if the questions were properly understood and also to collect critical remarks.

We defined a group of dyspeptics on basis of the most accepted criteria and decided to have a low grade of selection on severity of these criteria. The intention was to examine all dyspeptics with exception of those having an established diagnosis which we at that time meant could explain their dyspeptic symptoms. Foremost, we thought of peptic ulcer, gallstones and kidney stones. We wanted to compare the findings in subjects with dyspepsia with findings in subjects without these criteria of dyspepsia.

We wanted to have controls without dyspepsia, partly to open for the possibility to do a case-control study, partly as a basis for a possible cohort study. We chose to match controls regarding 10 -years age-group and gender.

2.6.1. The questionnaire survey.

Demographic data of all inhabitants of Sørreisa 20 years or older on December 31. 1986 were delivered from Kommunedata Nord-Norge. A postal questionnaire was sent to every third person on the list on March 25. 1987. On April 21. the questionnaire was sent to every second person of the remaining persons on the list, and the rest of persons had the

questionnaire sent on Mai 11. 1987. People not responding within 2 weeks got a postal reminder. People not answering after one month got a second postal reminder and a telephone call from one of our nurses shortly thereafter. At this call, we became aware of people not wanting to respond of religious reasons, we also got information of people working on ships or in distant regions making it difficult for them to respond. The nurse (Martha Øvermo) had worked for several years in the community health system as a health visitor and had been active in a Maternal and Child Health Centre. She had a thorough knowledge of people in the community and was highly respected. I assume that her presence, together with the other nurses, gave the project a confidence-inspiring face.

The questionnaire was followed by an introductory letter to the participants explaining the reasons for and the aims of the study. The letter clearly emphasised the scientific character of the study. A total of 119 questions assigned to the following 13 blocks: personal data, complaints of digestion, use of medication, former gastroenterological diseases, other complaints and former diseases, data about first degree family members with dyspeptic complaints and peptic ulcer disease in these members, eating habits, diet, leisure physical activity, use of stimulants like coffee tea, use of tobacco, use of alcohol, use of medicines, occupational

relations and finally recent social conditions and economical conditions during childhood.

All incoming answers were recorded at the Institute of Community Medicine at the University of Tromsø in a registration program which had been developed at the University hospital in Tromsø. All registrations were in a later procedure controlled to be in accordance with the actual questionnaires. The data were later on transmitted in an anonymised form to the SPSS-X statistical program for further evaluation and analysis.

2.6.2. The matching procedure

All of the subjects answering positively to the following two questions: «Have you ever had abdominal pain of at least two weeks duration?» and « If yes,was the pain located to the upper abdomen?» or to the question: «Have you ever had heartburn or acid regurgitation almost daily for at least one week? were defined as having dyspepsia. Potential controls were persons answering «no» to the first and the last question. Persons meeting the inclusion criteria as dyspeptics were matched with controls for sex and 10-years age-group. The controls were found among all the potential controls by a standard data program for randomisation.

2.6.3. Clinical examination and blood sampling.

All subjects were weighed. After this procedure they could lay down and pulse, heart sounds were registrated. Neck and abdomen were palpated and only occasionally other clinical examinations were used. A blood sample was drawn, cooled and centrifuged and the serum stored in a freezer at minus 20 degree C.

2.6.4. The endoscopy survey.

We wanted to do an endoscopy of all dyspeptic subjects and matched controls. After evaluation of the questionnaires at the Institute of Community Medicine, dyspeptics and random age and sex-matched controls were included in a daily schedule and offered an endoscopy by a postal letter. Subjects could alter their appointment by telephone or by a letter. Persons who did not respond got one reminder pr telephone. The subjects met after an over night fasting, although, subjects meeting after noon could have a light breakfast in the morning. Before endoscopy, the subjects were instructed by the nurses not to reveal anything about possible symptoms or history of former disease. They were informed about the

procedure and after endoscopy informed of major findings like peptic ulcer. Before endoscopy they were offered an intravenous injection of diazepam 5mg and Xylocain jelly 2% to swallow.

Endoscopy

A fully equipped endoscopy laboratory was set up in the local health center. We were equipped with new Olympus fiber gastroscopes GIF type Q 20, an Olympus halogen light source type CLE 3 and an Olympus endocamera for pictures. We also had a mobile suction unit and special equipment for lavage and desinfection of the endoscopes and biopsy forceps. For desinfection we used a commercially available glutaraldehyde solution (Korsolin; Norforma, Rud, Norway). After endoscopy, the instruments used were instantly washed with soap water, water and than put into a desinfecton solution. After desinfection the instruments were washed with water and therafter all channels in the endoscopes were pertubed with 70 % alcohol.

The endoscopist was trained from 1975 in endoscopy both in national and foreign university laboratories of gastroenterology (Kommunehospitalet,Århus, Denmark and Ullevål sykehus, Oslo, Norway) through several courses in endoscopy

and had performed over 10 000 endoscopies and had trained new endoscopists. The nurses were trained at the University Hospital Laboratory of Gastroenterology in Tromsø. In setting up of the local endoscopy laboratory one senior nurse from this laboratory supervised the installation and the hygenic routines.

2.6.5. The histopathological examination

Biopsy specimens were taken from the distal and proximal duodenum, from the lesser and greater curvatures of the antrum and the corpus of the stomach and also from all lesions. The rutine biopsy specimens were placed on a millipore paper on one line in a fixed order, placed in a formalin tube and labelled with reference numbers. The specimens were fixed and prepared according to standard methods in the University laboratory of pathology in Tromsø. Sections of the specimens were stained with haematoxylin and eosin and periodic acid Schiff and Alcian blue and were examined by one pathologist (Leif Bostad). Biopsies from lesions were separately handled in the rutine laboratory of pathology. The pathologist had no clinical information on the subjects. The histological findings were both described in the usual rutine mode and the findings plotted in a scheme feasible for computer handling.

2.6.6 Microbiological examination

Biopsy specimens from the stomach, one from the lesser and one from the greater curvature in the antrum were placed in 0.5 ml of sterile glucose/saline solution (25 % glucose in 0.9 % saline solution), ground and all material was divided into two equal portions and each portion placed on one blood agar plate and one brain-heart infusion agar containing 5 % horse blood. The media were placed in a Gas Pack jar under microaerophilic conditions (by Gas generating box Campylobacter bioMerrieux) and cultured by 37^0 C. After 3 days, the jars were transported to a special laboratorium at the University of Tromsø were the specimens were further cultured. The number of colonies was evaluated on a semiquantitative scale: sparsely, medium and rich. After three to ten days, positive cultures were tested for urease, catalase and oxidase activities. Cultures were also Gram stained for microscopic examination. Diagnoses of Helicobacter pylori was based on the positive enzymatic reaction and a typical microscopical appearance after Gram staining. The microbiologist had no clinical information on the subjects.

2.6.7. The sereological examination

Serum samples from all endoscoped persons stored at minus 20° C were analyzed in the Microbiological Department of the Oslo City Hospital Ullevål by Ketil Melbye with ELISA teqnique and a commercial kit «PYLOSET» for Helicobacter pylori antibodies.

2.6.8. The examination of the medical records

Medical records for the total population of the study, both responders and non-responders were examined in the local Community Health Center. All subjects reporting a former peptic ulcer had local medical records. Dispite a thorough search for medical records in nabour municipalities and at the University Hospital in Tromsø, we found no records for 103 subjects, 12 of whom was included in the endoscopy population. We looked for information about consultations for dyspeptic symptoms and evidence of previously diagnosed peptic ulcers by barium studies or endoscopy. We also registered all records of patients seeing their doctor for dyspeptic symptoms.

2.6.9. Definitions

Dyspepsia: all persons meeting the criteria of ever having had pain in the upper part of the abdomen for at least two week's duration or heartburn or acid regurgitation almost daily during at least one week.

Non-ulcer dyspepsia: All persons from the endoscopic study having dyspepsia without a peptic ulcer, deformity of the duodenal bulb or endoscopic duodenitis of the duodenal bulb.

Peptic ulcer: All persons with a verified peptic ulcer diagnosed with x-ray, endoscopy or both. By the endoscopy study peptic ulcer was defined as mucosal defects with the typical endoscopic visible features of a peptic ulcer with a crater more than 5 mm i diameter. All peptic ulcers were in addition biopsied to confirm the ulcer histologically.

Gastro-oesophagal reflux-like (reflux-like) dyspepsia, Ulcer-like dyspepsia and dysmotility-like dyspepsia as defined by Colin-Jones et al in 1988 (3).

Prevalence: For the cardinal symptoms defining dyspepsia, we have used a life-time prevalence in asking people whether they

any time had the symptoms in question. Other prevalences are point prevalences as for endoscopically diagnosed peptic ulcers or other endoscopic findings. Peptic ulcer prevalence was calculated from all former and actual peptic ulcers in an overall prevalence.

3. LIST OF PUBLICATIONS

I. Bernersen B, Johnsen R, Straume B, Burhol PG, Jenssen TG, Stakkevold PA. Towards a true prevalence of peptic ulcer: The Sørreisa gastrointestinal disorder study.
Gut 1990;31(9):989-92.

II. Bernersen B, Johnsen R, Straume B. Non-ulcer dyspepsia and peptic ulcer-Their distribution in a population and their association to risk factors.
Accepted for publication in Gut 1995.

III. Johnsen R, Bernersen B, Straume B, Førde OH, Bostad L, Burhol PG. Prevalences of endoscopic and histological findings in subjects with and without dyspepsia.
BMJ 1991;302:749-52

IV. Bernersen B, Johnsen R, Straume B, Burhol PG. Erosive prepyloric changes in dyspeptics and non-dyspeptics in a defined population.
Scand J Gastroenterol 1992;27:233-7.

V. Bernersen B, Johnsen R, Bostad L, Straume B, Sommer AI Burhol PG. Is Helicobacter pylori the cause of dyspepsia?
BMJ 1992;304:1276-9

4. THE MAIN FINDINGS

4.1. The prevalence of dyspeptic symptoms, non-ulcer dyspepsia and peptic ulcer.

Dyspepsia, according to the definition on page 22, was reported by 30.4 % of the men and 24.1 % of women. Frequency of dyspepsia increased slightly with age in men, unlike in women where dyspepsia was evenly distributed over all age groups. Stratified for age there were no significant differences in the occurrence of dyspepsia between the genders.

Non-ulcer dyspepsia was estimated to have a prevalence of 12.4 % in men and 13.5 % in women. The prevalence of non-ulcer dyspepsia was the same in both genders and seemed constant up to the age of 60. Above this age there was a marked decrease in the occurrence (paper II).

The prevalence of peptic ulcer was estimated on basis of reports from the questionnaire verified in medical records, endoscopy of all dyspeptics and controls by a calculation procedure accounted for in paper I. One crucial point in the estimation of peptic ulcer is the registration of ulcer scars (foremost deformed duodenal bulbs). The prevalence of reported peptic ulcers was 6.2 % in men and 2.7 % in women.

The point prevalence of peptic ulcer in the endoscopic study was lower in men (3.6 %) than in women (4.3 %). And the prevalences of deformed duodenal bulbs were also lower in men than in women, 5.9 % and 6.5 %, respectively. Estimated overall prevalences when deformed duodenal bulbs were calculated as former ulcers, were 10.5 % in men and 9.5 % in women, a statistically non-significant difference. At the endoscopy study we found a point prevalence of peptic ulcer in non-dyspeptics of 1%, higher in women than in men (paper I). Peptic ulcer was rare among people under the age of 40 years in men and under 50 years in women. The mean age of subjects with peptic ulcers in the endoscopic study was 45.8 years for men and 45,6 years for women
(paper II).

4.2. Associations between dyspepsia, non-ulcer dyspepsia and peptic ulcer and risk factors.

Comparing the associations of reported dyspepsia and non-ulcer dyspepsia with several demographic, life-style and social conditions we found about the same pattern of associations in both. The analysis of the association of dyspepsia to risk factors showed significant associations with sex, a family history of dyspepsia, peptic ulcer occurrence in

the family, smoking, previous smoking, frequent recurrence of herpes labialis and frequent health complaints. In the analysis of non-ulcer dyspepsia the associations were similar, but we here also found associations to the use of tranquillizers and to the feeling of lack of time. Reported dyspepsia was associated to smoking and previous smoking, non-ulcer dyspepsia was not.

The association of peptic ulcer with demographic, life-style and social conditions showed a pattern different from that of non-ulcer dyspepsia, firstly to age and gender, but also to smoking, a family history of peptic ulcer and feeling of stress, but also unexpectedly to having been breastfed as a baby. We also found significant associations with frequent recurrencies of herpes labialis and poor living conditions. In the light of the last years of Helicobacter pylori research we found it very interesting that both reporting frequent herpes labialis recurrencies and poor living conditions during childhood were risk factors for having Helicobacter pylori infection. Study of risk factors showed that both dyspeptics and non-dyspeptics had altered their habits. Teadrinkers controlled for earlier coffee drinking showed that 38 % of dyspeptics and 21 % of non-dyspeptics had stopped coffee drinking (paper II).

4.3. The endoscopic and histological findings

When all criteria for pathological findings, according to the applied definition used, were pooled together, only 10 % of both subjects with and without dyspepsia had a normal gastric and duodenal mucosa. Out of five endoscopic and four histological diagnoses, only peptic ulcer, endoscopic duodenitis and active chronic gastritis were diagnosed significantly more often in subjects with dyspepsia compared to non-dyspeptics. Of histological diagnoses, only active chronic gastritis was more frequent in dyspeptics than in controls. A substantial amount of 50 % of controls had chronic atrophic gastritis, and 20 % of peptic ulcer was found among controls (paper III).

Erosive prepyloric changes (EPC) were described by Nesland and Berstad 1985 (16) as deviations from the normal mucosa, with standing mucosal folds, sometimes with red spots and streaks and sometimes in addition erosions, divided into 3 degrees. In our study we found EPC in 38.5 % of dyspeptics and 35.1 % of non-dyspeptics, in both groups more frequent in men than in women. Occurrence of Helicobacter pylori was not associated with occurrence of EPC. Endoscopic duodenitis was found more frequently in subjects of the two highest gradings of EPC, and the highest grading was associated with chronic

gastritis. EPC was associated with smoking and in women, in addition, with use of alcoholic beverages (paper IV).

4.4. Helicobacter pylori

Helicobacter positive cultures were found more often in subjects with dyspepsia (48%) than in subjects without dyspepsia 36%. Positive culture in both subjects with and without dyspepsia was strongly associated with histological gastritis and peptic ulcer. Only 3 % of subjects with a histologically non-inflamed gastric mucosa had this infection (paper V).

Further studies on this material as yet unpublished, shows that H. pylori positive cultures, when semiquatitatively graded, are for the highest grade found significantly more often in dyspeptics than in non-dyspeptics. Of dyspeptics 96, and of non-dyspeptics 59 subjects had this highest grade of H. pylori growth (Table 1). We found significant differences in frequency of oesophagitis between dyspeptics and non-dyspeptics 11.5% and 3.4 %, respectively, and we also found a in frequency of endoscopic duodenitis with 24.0% and 6.8 %, respectively. When histological diagnoses were analysed for this group of H. pylori positive subjects, there were no differences between dyspeptics and non-dyspeptics (Table 2).

Unfortunately, we had no help from sereological studies in evaluating the H. pylori infection because of poor specificity. We do not know the cause of this result, but at least one reason may be cross reactions to campylobacter jejuni antibodies.

4.5. The clinical examination

We searched for tender points in the abdomen by palpation and let the subjects eventually point them out, but we found no association between tenderness in the upper abdomen and peptic ulcer or duodenitis.

By the clinical examination of the abdomen we found one middle aged woman and five middle-aged men having an enlarged liver. Two women had situs inversus, one at the age of 68 years who knew of her situs inversus and one 22 year old woman who remembered her mother mentioning something of her heart beeing located on the right side. A 66 year old man had an aortic aneurism which was confirmed by aortography at the University Hospital in Tromsø. Due to the lack of surgical capacity, he was discharged, and a month later successfully treated in an emergency operation after rupture of his aneurism. Another woman had a greenish corneal ring, best

fitting the discription of a Kaiser-Fleischer ring, but without corresponding clinical or biochemical findings.

5. GENERAL DISCUSSION

5.1 Methodological considerations

This population based study of dyspepsia, peptic ulcer and endoscopic findings has several advantages; a substancial response rate of 88.9 % on the questionnaire survey and an attendence rate of 79 % in the endoscopy study, a diagnostic endoscopy performed in both dyspeptics and non-dyspeptics, blinding of all diagnostic procedures, and unique possibilities for search in medical records for the results of previous diagnostic examinations. Despite the high response rates there are still some non-responders, and any chosen definiton of dyspepsia for endoscopy would represent a potential for selection bias. We chose to reveal the whole "ice-berg" of symptoms and clinical findings without selection on severity of symptoms. We tried, however, to keep the definition of dyspepsia within the frames of international accepted definitions. The main methological weaknesses of this study are the lack of dimensions on intensity of symptoms, whether the reported dyspepsia represented current complaints, and the cross sectional design. Other problems are the selection bias for endoscopy by exclusion of subjects with self-reported peptic ulcers and the lack of assessments of

inter-and intra-obserer variation. The first two problems will be discussed in the chapter: Dyspepsia and endoscopic and morphological findings (5.2.2.on page 50).

Non-response is a modest problem for the conclusions of this study. Among the non-responders we had an overrepresentation of the youngest age group and an underrepresentation of the age group 50-69 years both in men and women. By examination of the local medical records, we found significantly fewer peptic ulcers in this group than among responders. From these data it may be assumed that the non-responders had fewer problems related to the gastrointestinal tract and thus were less motivated for participation in this survey. Especially, among young people, there were some persons working outside the community where they may have had their health service, but, unfortunately, we do not have information about this group. There was also a small group of religiously active people (Maran Ata) not participating of religious causes. The local church authority had listed approximately 20 people of this religious congregation. Several non-responders are sailors or people temporaryly working outside the hometown. Presumeably this latter group consists of people disposed to dyspeptic symptoms. We have, however, no information about complaints and diseases in this group.

Subjects who reported peptic ulcer disease, were in our design excluded from the endoscopy study. We supposed that these subjects had had some diagnostic procedures with peptic ulcer as the explanation of their symptoms. As our capacity for endoscopy was restricted, we considered a new endoscopy of these subjects of less importance compared to the possibility to endoscope undiagnosed subjects with dyspepsia. The exclusion of this group of dyspeptics represent a potential selection bias which must be taken into consideration when comparing findings in dyspeptics and non-dyspeptics. This group of dyspeptics may have had a higher score of pathological endoscopic and histological findings. However, would also their potential controls have had a substantial amount of pathological findings, peptic ulcer included.

5.1.1. The cross sectional design

The cross-sectional nature of this study makes it impossible to study causality. The study has, however, been used to eluciate and question some conventional conceptions. In our cross-sectional perspective of the population of Sørreisa, we have used gross characteristics as sex and age. Use of more sophisticated parameters may, however, be

difficult. Even generally accepted risk factors could be disturbed in a cross-sectional design due to change of habits. An example is our findings of coffee and tea-drinking in relation to dyspepsia. Special groups of a population may be more aware of possible risk behaviour, which is then readily altered when symptoms or suspicion of disease comes up.

5.1.2. Reporter bias.

We had no possibility to estimate the magnitude of reporter bias except for the reporting of peptic ulcer. By searching all local medical records, we were unable to confirm 15.3 % of men's reports of peptic ulcer and 20.3 % of the corresponding reports in women. For false negative reports the numbers were 1.3 % and 0.2 % in men and women, respectively. It must be pointed out that all persons reporting an ulcer had been admitted to a diagnostic procedure with x-ray or endoscopy or both, so that their reports of having peptic ulcer may merely be a matter of a communication problem, or perhaps an example of over-interpretation of findings.

Medical records for 103 persons were not at hand, which we regarded negligible in this context. None of those reporting peptic ulcers were among those with missing records.

5.1.3. Observer bias

The main objections to the presented results are the possibility of observer bias. The endoscopic study was performed with the endoscopist blinded for whether he examined a subject with or without dyspepsia. The blinding procedure was performed successfully with the cooperation and understanding of every person endoscoped. All specimens, whether sent to histopathology or to microbiology, were identified with numbers. These were all procedures designed to avoid observer bias. However, all the interpretators were aware of the design of the study and that the examined specimen was from a study participant. The effect of this knowledge on the diagnostic results is unknown. No procedure addressing on inter-intra-observer variation was planned, but would not have given relevant information about such potential bias, because all participants would have been informed of the scientific nature of this study. However, unintentionally, we have got the opportunity to compare different examination procedure of Helicobacter pylori (Table 1 and 3). Table three indicates some disagreement in the morphological identification of H. pylori between the two pathologists. The interpretations showed both, a significant but opposite difference between dyspeptics and non-dyspeptics. Not

surprisingly, most of the disagreement was connected to the interpretations of the culture negative specimens and those with a corresponding low graded growth (table 3). The proportional agreement for diagnosis of H. pylori from specimens with growth graded II or III was very good. Using cultures as a reference standard, the main problem of morphological diagnosis of H. pylori seems to be the amount of false positive H. pylori diagnoses and a corresponding low specificity. It is again an important reminder for including inter-intra-observer studies when clinical observation is used as basis for dagnosis. Fortunately, all observations and diagnosing in this study were performed blindly, and should therefore not have interferred on the distribution of findings between dyspeptics and non-dyspeptics.

5.2. Discussion of some main findings.

5.2.1 The occurrence of dyspeptic symptoms and their pattern in the general population.

The main dyspeptic symptoms usually ascribed to the upper gastrointestinal tract are epigastric pain (in its classical form relieved by drinking milk or by eating), sometimes occuring during the night, and heartburn, aggravated by

stooping or by laying in flat posture. Different from these symptoms are symptoms usually refered to the lower abdomen as low abdominal pain, diffuse abdominal pain usually combined with bloating, early satiety, nausea and alternating constipation and frequent loose stools. The key symptoms were in this study epigastric pain and heartburn. It is therefore interesting to notice that concomitant symptoms to pain, were reported at the same level in association with abdominal pain and diffuse pain, as to epigastric pain and heartburn (Table 5). So the pattern of reported symptoms did not indicate a special «upper gastro- intestinal tract» pattern. The predictive properties of epigastric pain and heartburn are, however, not better regarding organic diseases than are combination of symptoms with abdominal pain of any location (14,22).

Most people with dyspepsia do not have severe organic diseases and a great proportion of people with gastritis or H.pylori infection do not have symptoms. There have been attempts to group specific symptom complexes, like that of the working party for management of dyspepsia around Colin-Jones (3). Patients without a peptic ulcer or other major pathological findings (endoscopy negative dyspepsia) are grouped into different syndromes according to cardinal

symptoms, like: reflux-like dyspepsia, dysmotility-like dyspepsia, ulcer-like dyspepsia.

Reasons for grouping symptoms into syndromes might be:

1) The groups reflect patterns found in the patient populations.
2) The syndromes represent entities carrying prognostic knowledge.
3) The syndromes could reflect knowledge of aetiology and/or pathogenesis.

For the definitions used by the group around Colin-Jones, the last two assumptions are in my opinion not fulfilled, but will not be further discussed in this context. Regarding patterns of dyspeptic symptoms found in a general population, several authors have questioned the classification of non-organic dyspepsia; Talley among others could not recognise the defined entities in the population of Olmsted County, Minnesota. He also pointed out that patients having symptoms consistent with one group, could be classified in more than one group (9). These objections against an exclusive classification of dyspeptics in one group is supported by the Sørreisa data (table 6). As Talley has shown, there are difficulties in recognising the pattern of dyspeptic syndromes. Among the persons with reported symptoms in accordance with any of the

syndromes, many persons had symptoms which could be placed in several syndromes (Table 6). Lastly the number of persons not «fitting in» in any of the syndromes amounts to 70 % (Figure 1) of the syndromes.

The dyspeptic symptoms overlap and a substantial amount of persons could be allocated to several groups, or the patterns of symptoms did not fit to any group of syndromes.

One objection to the findings is the lack of relevance. The people are not patients, and the pattern among patients would be different. Both patients and the doctors use their preconceived (often anecdotal) knowledge, and therefore their symptom patterns may represent a selection bias, a self reinforced circle arguing. On the other hand we had the possibility to do subanalysis on people visiting the primary physician the last year, those referred to hospital due to abdominal pain and those without contacts with the formalised health care system. There are no differences between the three groups regarding reported patterns of symptoms.

So far, it seems important to identify persons with organic diseases as H. pylori related disease and serious reflux disease which could be treated successfully. Of course malignancy should be recognised, but the rest of the persons with dyspeptic complaints should be reassured and guided regarding lifestyle, diet habits and coping strategies.

5.2.2. Dyspepsia and endoscopic and morphological findings.

The association between different types of gastritis and symptoms has been questioned by several authors (18,23). But the belief in duodenitis as a clinical entity has been strong, and especially morphological duodenitis grade II and III have been recognised as a disease (24,25). Erosive prepyloric changes (EPC) have been claimed as a new disease entity, especially in Scandinavia (26). There have been several critical voices against also this clinical entity.

Except from endoscopic duodenitis and peptic ulcer disease, the endoscopic study in Sørreisa do not support any theories of these entities being diseases associated with dyspeptic symptoms. There are, however, several objections against the findings, all based on the applied definition of dyspepsia. Our definition did not take into account neither the intensity nor the duration of dyspeptic symptoms. The reported symptoms also do not need to be current symptoms.

Unfortunately, we do not have information about the intensity of the symptoms, but indirectly we have some information about the seriousness or grading, as judged by the patients. An indication on the seriousness of the symptoms are the reports on consulting the local health care service due to epigastric pain (table 6). Subanalysis of the number of

persons who had been in contact with the local health care the last year due to epigastric pain, showed the same findings regarding association between symptoms and endoscopic findings as in paper III-Table II. Minor symptoms do not seem to be an acceptable explanation of our findings.

We also have met criticism of the use of dyspeptic symptoms not being current symptoms. When analysing endoscopic and morphological findings in relation to defined dyspepsia and to epigastric pain the last two weeks, there are no significant differences from the results presented in paper III (Table 7).

In conclusion, we may claim that it is unlikely that our findings can be explained by selection of subjects without current symptoms, transitoric symptoms or minor symptoms which usually are not sufficiently alarming to release a consultation of the physician. Our findings should inspire gastroenterologists to control our findings for the purpose of avoiding further unnecessary non-disease labels given the explanatory function of dyspeptic symptoms.

5.2.3. Helicobacter pylori

The spiral bacteria which could be seen in the stomach mucosa were for a long time left out of consideration as a pathogen, probably because it was difficult to culture and study the bacteria. Now the diagnosis of H. pylori infections seems to be a matter of routine. Authors agree that testing or growing tissue from the stomach mucosa is an excellent method of detection with a high specificity. Routine staining and special staining of biopsies are good methods, but may be less sensitive and less specific. Sereologic testing is today a simple and very sensitive method, although antibodies may remain for years after clearance of the bacteria. The urea breath test is now a very sensitive method of detection with a high specificity, but a grading of the bacterial growth or activity will be difficult(27).

In the Sørreisa survey we chose to culture biopsies for a specific diagnosis as a reference standard. Culture is, however, a difficult method and we know that bacterial growth can be hampered by transport, antibacterial agents or inadequate culture methods. Our results showed discrepancies between culture and morphological diagnosis. An exact diagnosis morphologically seems difficult with reference to the differences in diagnosis between pathologists. Sereology

was with the methods used in our material not sufficiently specific (table 1). This may be a problem in populations with a high frequency of campylobacter jejuni infection due to cross-reactions.

Our investigation shows that there is an association between the high grade of growth of H.pylori in our cultures and the morphologic diagnosis (Table 2).

We found only a week association between H.pylori infection and dyspepsia in our total material. The finding of a significant difference between dyspeptics and non-dyspeptics for only the highest grade of H. pylori growth from antral biopsies, may be a reason to reconsider our interpretation. There is in the highest grade of H. pylori growth a significant difference between dyspeptics and non-dyspeptics (table 1). Still one fifth of the non-dyspeptics had an infection with H. pylori where the growth was classified as grade III. For the lesser grades of growth there was no association to the dyspeptic symptoms. One may considerate whether activity or intensity of the infection could have some importance for the symptoms. It is also interesting that endoscopic duodenitis and oesophagitis are found significantly more often in dyspeptic subjects with H. pylori infection than in subjects without dyspepsia. If H.pylori is of etiologic or pathogenetic importance for peptic ulcer, then it is possible

that endoscopic visible duodenitis is a stage in the development of duodenal ulcer.

Our study has inspired us to question the up to date belief of H. pylori as the causal factor of peptic ulcer. We know from research over the past century that peptic ulcer disease must be multifactorial and that pepsin and acid secretion are crucial in the pathogenesis of the ulcer. At least one must admit that H. pylori infection and gastritis per se is a very common state, but only a small part of subjects with this infection will have a peptic ulcer. There must be another factor or several factors which activate the infection. In our material, we found different stages of H.pylori status. Firstly one stage with only morphological detection of the bacteria, one second stage with both positive culture, positive morphology and a high level of seropositivity and thirdly a stage only with positive serology. It may be possible that H. pylori infection which around the world is very common, at one stage or in some persons causes an immunological reaction which can develop into peptic ulcer or an atrophic gastritis.

6. EPILOGUE

6.1. Reflections about non-disease.

When looking back at the results of this study, one of the stunning observations was the great amount of ascribed pathology in apparently healthy people. At least one must admit that these persons did not report dyspeptic symptoms. Should these people of ethical reasons be informed of their pathology, and should these findings have consequences for counselling or therapy? What about patients seeking their doctor for dyspeptic symptoms? Does the finding of gastritis endoscopically or histologically explain their symptoms, and would any treatment directed against this inflammation be appropriate? Which lesson could be taught from the example of Erosive prepyloric changes (EPC).

In our material, there were no common gastrointestinal symptoms associated with EPC. It is tempting to call upon the thoughts of Meador some 30 years after his excellent paper on the art and science of non-disease (28). The temptation is to classify the histological diagnosis of duodenitis and gastritis as well to his class of Overinterpretations-of-physical-findings-syndrome or perhaps more specifically into the Overinterpretation-of-endoscopic-findings-syndrome. That

is the reason why our controls not should be named healthy controls, but more preferably non-dyspeptics. The described phenomena are not false positive findings, but irrelevant explanations of dyspeptic symptoms. It is the physicians task to take serious patients concerns due to symptoms. Labelling of symptoms, like gastritis, is in fact to create a non-disease, which in turn causes more distress and endless search for cures, supporting unserious participants of the authorised and non-authorised health market. This tendency can be observed in several fields where new diagnostic technology is applied, and new findings uncritically are accepted as a reason for complaints or dysfunction (29)

Before the medical society accepts any use of new therapeutic regimens, it legitimally asks for properly designed trials. Likewise, should the same society ask for specifically designed studies in advance before the interpretation of new technological findings are applied.

6.2. The importance of Helicobacter pylori

Helicobacter pylori (H. pylori) has in the opinion of very many researchers and clinicians got the status of the etiologic agent for gastritis, peptic ulcer and an important

role in the pathogenesis of gastric carcinoma. Most clinicians recommend to treat the infection in peptic ulcer patients. The effect will be a lower recurrence rate, especially for duodenal ulcer. The observations on recurrence of peptic ulcer published, have mostly covered one year. We do not know what happens to the peptic ulcer patients on a long term after H. pylori eradication. Eradication of H. pylori as a treatment of non-ulcer dyspepsia has given uncertain results, but may give symptom relief in subgroups of non-ulcer dyspepsia (30). The eradication of H. pylori will require the use of one or more antibiotics and maybe potentially toxic agents like bismuth. We also do not know the natural course of H. pylori infection and we do not know to what extent this infection in asymptomatic individuals will cause future clinical disease, but no experts have until this time recommended a prophylactic treatment of the infection, nor programmes to reveal such infections.

On the basis of our work, we would recommend to follow up H. pylori positive individuals both with and without symptoms for a long period to see to which extent asymptomatic individuals are converted into symptomatic ones and vice versa. It would also be interesting to see which individuals need further diagnostic procedures, namely to discover peptic ulcer disease.

6.3. Personal view

The Sørreisa Gastrointestinal disorder study has made it obvious to me that clinicians, every day presented to patients or persons suffering from symptoms, need to be aware of from which pond these symptoms are drawn. Which diseases would these symptoms match, and if these symptoms are an expression of disease? Introduced to fancy and sophisticated tools aimed at detecting disease, we have to be cautious not to give the conditions found the disease-label and in the next moment give our findings the authorisation of an explanation of the symptoms of the patient. Surely is this an old knowledge for clinicians, but examples from my own clinical field show that we have to be very conscious, not to fall into this pitfall.

This study was planned with certain ideas in mind originated in clinicians. We wanted to see which dyspeptic symptoms we could find in an unselected population and which associations they had to disease. We chose to set the focus on dyspepsia compared to the condition of having no dyspepsia. This design of our study has given answers in relation to dyspepsia, but we might as well have done an endoscopy of a random sample of the population. That would have given us the possibility of a wider perspective. Those thoughts are,

however, a belated wisdom and without this study at that particular time, we might not even today have been the owners of that wisdom.

It would be very interesting to see the Sørreisa-population once more. It would be very interesting to see, after a suitable time, what has happened with the dyspeptic persons without disease in 1987. How have dyspeptic symptoms developed? Have some of them got a peptic ulcer disease and who got this disease? Was getting peptic ulcer disease related to any of the factors recorded in 1987? Has Helicobacter pylori been of significance? What has happened to the persons with a peptic ulcer before 1987? Have they suffered from complications? We would also ask those groups of their use of health services and use of medication. How was the development in the healthy controls? Did any of them develop symptoms or disease, and, was in that case disease or symptoms related to factors recorded in 1987, especially to Helicobacter pylori infection?

7. REFERENCES

1. Nyrén O. Non-ulcer dyspepsia. Studies on epidemiology, pathophysiology, and therapy. Dissertation (Acta Universitatis Upsaliensis 527). Uppsala 1985.
2. Nyrén O, Adami HO, Bates S, et al. Abscence of therapeutic benefit from antacids or cimetidine in non-ulcer dyspepsia. N Engl J Med 1986;314:339-43.
3. Colin-Jones DG, Bloom B, Bodemar G, Crean G, Freston J, Gugler R, Malagelada J, Nyrén O, Petersen H, Piper D. Management of dyspepsia: Report from a working party. Lancet 1988;1:576-9.
4. Jones R, Lydeard S,E, Hobbs FDR et al. Dyspepsia in England and Scotland. Gut 1990;31:401-5.
5. Tibblin G. Introduction to the epidemiology of dyspepsia. Scand J Gastroenterol 1985;20(suppl 109):29-33.
6. Talley JN, Phillips SF. Non-ulcer dyspepsia: Potential causes and pathophysiology. Ann Intern Med 1988;108:865-79
7. Brummer P, Häkkinen I. X-ray negative dyspepsia. A follow-up study. Acta Med Scand 1959;165:329-32.
8. Krag E. Pseudo-ulcer and true peptic ulcer. A clinical, radiographic and statistical follow-up study. Acta Med Scand 1965;178:713-28.

9. Talley NJ, Zinsmeister AR, Schleck CD, Melton III LJ. Dyspepsia and dyspepsia subgroups: A population-based study. Gastroenterology 1992;102;1259-68.

10. Greenslaw R, Sheahan DG, DeLuca V, Miller D, Myerson D, Myerson P. Gastroduodenitis. A broader concept of peptic ulcer disease. Dig Dis Sci 1980;25(9):660-72.

11. Owen D. The diagosis and significance of gastritis. Pathology Annual 1979;1:247-71.

12. Moynihan BGA. On duodenal ulcer; with notes of 52 operations. Lancet 1905;I:340-6.

13. Heatley RV, Rathbone BJ. Dyspepsia: A dilemma for doctors. Lancet 1987.ii:779-82.

14. Johannesen T, Petersen H, Kleveland PM, Dybdahl JH, Sandvik AK, Brenna E, Waldum H. The predictive value of history in dyspepsia. Scand J Gastroenterol 1990; 25:689-97.

15. Hertzman P, Jönsson B, Lindgren B: The economic costs of ulcer disease. The Swedish Institute for Health Economics Report 6, Lund 1979.

16. Adami HO, Agenäs I, Gustasson S, Lööf L, Nyberg A, Nyrén O. Tyllström J. The clinical diagnosis of «gastritis»: aspects of demographic epidemiology and health care consumption based on a nationwide sample survey. Scand J Gastroenterol 1984;19:216-19.

17. Wolf S. The psyche and the stomach. Gastroenterology 1981;80:605-14.

18. Siurala M, Isokoski K, Kekki M. Prevalence of gastritis in a rural population. Bioptic study of subjects selected at random. Scand J Gastroenterol 1968;3:211-23.

19. Warren JR, Marshall B. Unidentified curved bacilli on gastric epithelium in active chronic gastritis. Lancet 1983;I:1273-5.

20. Wood JR, McIsaac RI: Histamine H_2-receptor antagonists in the treatment of peptic ulcer disease. South African Med J 1988;74:51-4.

21. Consensus conference. Helicobacter pylori in peptic ulcer disease. JAMA 1994;272:65-9.

22. Klauser AG, Voderholzer WA, Knesewitsch PA, Schindlbeck NE, Müller-Lissner SA. What is behind dyspepsia? Dig Dis Sci 1993;38:147-54.

23. Cheli R, Perasso A, Giacosa A. Dyspepsia and chronic gastritis. Hepato-gastroenterol 1983;30:21-3.

24. Whitehead R, Roca M, Meikle DD, Skinner J, Truelove SC. The histological classification of duodenitis in fiberoptic biopsi specimens. Digestion1975;13:129-36.

25. Sircus W. Duodenitis: A clinical, endoscopic and histopathologic study. Quarterly J Med 1985;221:593-600.

26. Nesland AA, Berstad A. Erosive prepyloric changes in persons with and without dyspepsia. Scand J Gastroenterol 1985;20:222-8.

27. Peura DA. Helicobacter pylori: Practical guidelines for diagnosis and treatment. Gastroenterologist 1993; 1(4):291-5.

28. Meador CK. The art and science of nondisease. N Engl J Med 1965;272(2):92-95.

29. Gutknecht DR. Meador revisited: Nondisease in the nineties. Ann Intern Med 1992;116(10):873-4.

30. O'Connor HJ. eradication of Helicobacter pylori: Therapies and clinical implications. Postgrad Med J 1992;68:549-57.

8. TABLES AND FIGURE

Table 1: The frequencies (%) of Helicobacter pylori identified by different methods in dyspeptics and non-dyspeptics. Sørreisa 1987/88.

	Dyspeptics (N=309)		Non-dyspeptics (N=310)	
Identification methods	n	%	n	%
Cultures of biposies:				
- growth graded I	21	6.8	24	7.7
- growth graded II	30	9.7	29	9.4
- growth graded III	96	31.1	59	19.0*
- total	147	47.6	112	36.1*
Morphology:				
- pathologist I	194	62.8	162	52.3*
- pathologist II	164	53.1	128	41.3*
Serology:				
- Pyloset	180	58.3	183	59.0
- Igg7#	234	75.7	217	70.0
- Igg8#	215	69.6	191	61.6
- Igg9#	179	57.9	165	53.2

#The figure indicates the titer where the threshold for positive test was set.
*p<.01

Table 2: The frequencies of some endoscopic and histological findings among the endoscoped persons with growth of grade III of Helicobacter pylori. Sørreisa 1987/88.

	Dyspeptics (N=96)		Non-dyspeptics (N=59)		
Endoscopic diagnoses:					
	n	%	n	%	p-value
Oesophagitis	11	11.5	2	3.4	.04
Superficial gastritis	22	22.9	9	15.3	.25
Atrophic gastritis	7	7.3	1	1.7	.12
Peptic ulcer disease	8	8.3	2	3.4	.22
Duodentitis	23	24.0	4	6.8	.006
Histological diagnoses:					
Chr. atrophic gastritis	87	90.6	53	89.8	.87
Active chr. gastritis	35	36.5	22	37.3	.91
Duodenitis	65	67.7	45	76.3	.25
Metaplasia	31	32.3	16	27.1	.49

Table 3: Agreement between two pathologists of morphological Helicobacter pylori diagnosis, expressed as proportional agreement according to graded growth of Helicobacter pylori. Sørreisa 1987/88

Cultured antrum biopsies for H.pylori.	proportional agreement
-negative culture	.77
-growth graded I	.71
-growth graded II	.84
-growth graded III	.89

Table 4: The distribution (%) of reported abdominal complaints by nature and location (N=436) among men and women aged 20-69 years. Sørreisa 1987.

	Epigastric pain (N=215)*	Low abdominal pain (N=91)*	Diffuse abdominal pain (N=115)*
Duration of daily pain >2 months	27.4	33.3	46.4
Pain during the night	36.2	27.1	45.9
Heartburn or acid regurgitation	50.2	24.2	46.1
Frequent nausea	16.7	18.7	23.5
Early satiety	17.1	4.4	20.0
Meteorism	70.7	67.0	80.9
Relief of symptoms by defecation	83.6	80.3	83.9
Obstipation	20.0	20.9	23.5
Reporting two or more extra-abdominal complaints**	23.3	31.0	39.1

* The denominator varies due to missing answers.
** Based on reports of frequent suffering from headache, dizziness, palpitations, sleeping disturbances, joint and muscle pain.

Table 5: Frequency (%) of different categories of dyspepsia by combinations of the same main categories in subjects aged 20 to 69 years. Sørreisa 1987.

Category of dyspepsia like		Ulcer-like (N=39) %	Reflux-like (N=120) %	Dysmotility-like (N=219) %
Combinations	n			
Reflux-like and ulcer-like	(31)	79.5	25.8	-
Ulcer-like and Dysmotility-like	(23)	59.0	-	10.5
Reflux-like and Dysmotility-like	(54)	-	45.0	24.7
All three categories	(20)	51.3	16.7	9.1

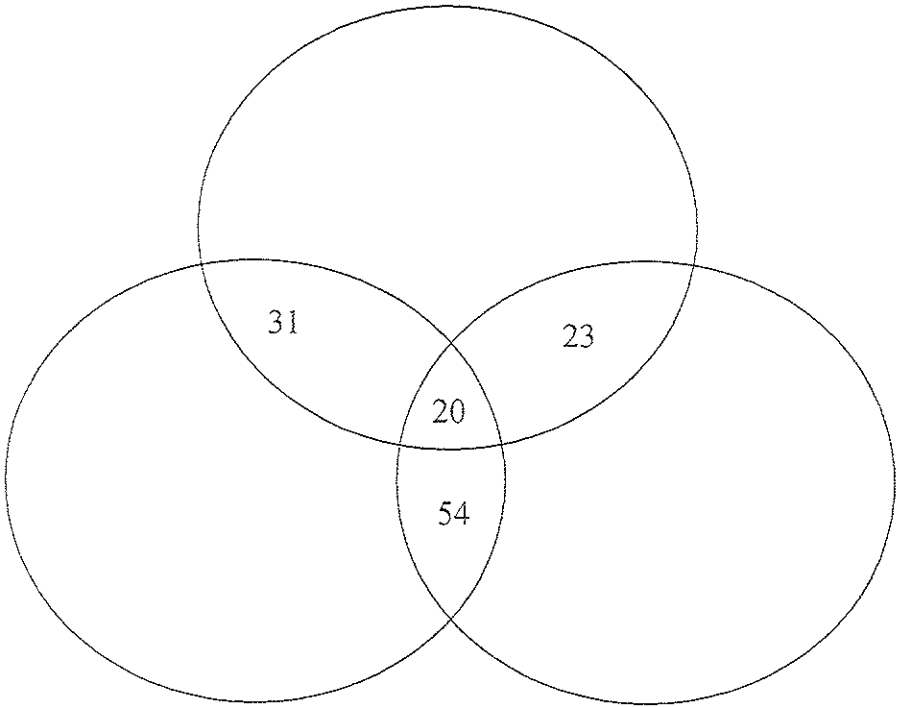
Table 6: The frequency (%) of use of health care and use of medication by location of reported pain (N=436) among men and women aged 20-69 years. Sørreisa 1987.

Localisation of pain	Epigastric (N=215)* %	Low abdominal (N=91)* %	Diffuse abdominal (N=115)* %
Duration of daily pain >2 months	27.4	33.3	46.4
Visiting the local physician the last year	82.9	85.2	84.1
Referred to specialist due to pain the last year	54.5	51.7	56.5
Medical certificate/sick leave	21.8	25.3	32.7
Used antacids	75.4	43.2	66.1
Used H-2 blockers	40.6	14.8	41.5

* The denominator varies due to missing answers.

Table 7: Prevalences (%) of endoscopic and histological findings in dyspeptics by current dyspepsia and by previous dyspepsia. Sørreisa 1987. (From Roar Johnsen: Population studies on dyspepsia and peptic ulcer disease. Tromsø 1992)

	Epigastric pain last two weeks (N=84)	Previous dyspeptic symptoms only (N=225)	p-value
Endoscopic findings			
Oesophagitis (grade I or II)	13.1	11.2	.63
Superficial gastritis	22.6	19.2	.61
Duodenogastric reflux	20.2	16.1	.49
Peptic ulcer disease	10.7	8.0	.46
Duodenitis	17.9	23.2	.31
Normal endoscopy	54.8	52.7	.74
Histological findings			
Chronic superficial gastritis	34.5	46.4	.06
Chronic atrophic gastritis	54.8	63.8	.15
Active chronic gastritis	25.0	25.0	1.00
Duodenitis	73.8	58.5	.01
Duodenitis grade II	32.3	35.1	.70
Normal histology	11.9	13.4	.73
Normal endoscopy/histology	9.5	10.7	.76


Ulkus-lignende dyspepsi N=39
31
23
20
54
Refluks-lignende
Dysmotilitets-lignende

9. PUBLICATIONS

PAPER I

Gut, 1990, 31, 989–992

Towards a true prevalence of peptic ulcer: the Sørreisa gastrointestinal disorder study

B Bernersen, R Johnsen, B Straume, P G Burhol, T G Jenssen, P A Stakkevold

Abstract

This study, designed to overcome methodological problems inherent in earlier prevalence studies of peptic ulcer, was carried out in a municipality in northern Norway. It included the total population of 2027, aged 20–69 years, and comprised a questionnaire and search for previously diagnosed peptic ulcers in the local medical records for all subjects, and additional endoscopy of all subjects with dyspepsia and their matched healthy controls (n=619). The overall prevalence was 10·5% in men and 9·5% in women, a sex ratio close to one and a higher duodenal:gastric ratio than previously reported from this region. A substantial 1% prevalence of asymptomatic ulcers was also observed.

'Tell me, sweet lord, what is't that takes from thee thy stomach, pleasure, and thy golden sleep?' says Lady Percy to her husband Henry. Not only does classical literature, like Shakespeare's *Henry IV*, link gastric disorders to men, medical reports also identify peptic ulcer as a male infirmity.

During the past 40 years, studies have consistently shown higher prevalences in men for both gastric and duodenal ulcer.[1–4] Kurata, however, has reported a decline in sex ratio of self-reported peptic ulcers in the USA to 1:1.[5] The prevalence of duodenal ulcer seems to vary considerably around the world, but it generally occurs more frequently than gastric ulcer.[1–3] Studies in Scandinavia have shown gastric ulcer to be more common than duodenal ulcer in the northern part,[6–8] whereas duodenal ulcer dominates in the southern part.[9–11] Only one study from Malmø in southern Sweden, which was based on necropsy examinations, showed a higher prevalence of gastric than duodenal ulcer in both men and women.[12]

Studies on the occurrence of peptic ulcer that use patients' records are hampered by considerable biases. Selection takes place both by patients with dyspepsia deciding whether or not to present their problems to the physician and by physicians deciding whether to refer their patients for further diagnostic procedures. Moreover, surveys where the diagnosis of peptic ulcer depends on symptoms are complicated by the fact that some peptic ulcers are asymptomatic.[13]

The purpose of this population based study was to establish an overall prevalence of peptic ulcer, both for symptomatic and for asymptomatic ulcers, by combining a lifetime prevalence from questionnaire reports and examination of available medical records together with a point prevalence from endoscopy of subjects both with and without dyspepsia. The study endeavoured to get closer to the true prevalence of peptic ulcer disease.

Material and methods

This study was carried out in the municipality of Sørreisa in northern Norway (latitude, 69° north). The town has 3500 inhabitants and is in a rural area with a local administration centre. The principal occupations are agriculture and wood-processing and service industries, a distribution of occupational groups close to the average for Norway. From March to May 1987 all inhabitants born between 1917 and 1967, 2027 men and women, received a postal questionnaire with 119 questions on abdominal complaints, health, lifestyle, diet, and social conditions.

Subjects with positive responses to the first two or the last of the following questions, or both, were considered to have suffered dyspepsia:

Have you ever had abdominal pain of at least two weeks' duration?

If yes, was the pain located to the upper abdomen?

Have you ever had heartburn or acid regurgitation almost daily for at least one week?

Those who had had dyspepsia but no prior history of peptic ulcer, gall stone, kidney stone, cardiac diseases, or abdominal surgery were offered endoscopy. Corresponding asymptomatic controls matched for sex and age (within the same 10 year age group) were randomly selected and offered an endoscopy as well. Controls who refused endoscopy were replaced by a second, similar procedure. Ten pregnant women were excluded from endoscopy, and in the following analysis they were included in the refuser group.

The Figure summarises the study procedures. Of 495 subjects with dyspepsia, 137 were excluded. Of 782 subjects invited to have endoscopy, 309 dyspeptics and 310 controls underwent gastroscopy. The subjects were endoscoped within one month of returning their questionnaires, and after first giving their informed consent.

All endoscopies were performed by one of the authors (BB), who is a trained endoscopist. The examinations were carried out at the local health centre with Olympus gastroscopes GIF Type Q 20. The endoscopist was blinded in the sense of not knowing whether or not he was examining subjects with dyspepsia or controls.

A gastric or a duodenal ulcer was diagnosed if an ulceration greater than 0·5 cm was seen proximally or distally to the pylorus, respectively. Deformity of the duodenal bulb was considered to be present when flattening, scars, stenosis, or narrowing of the bulb was seen.

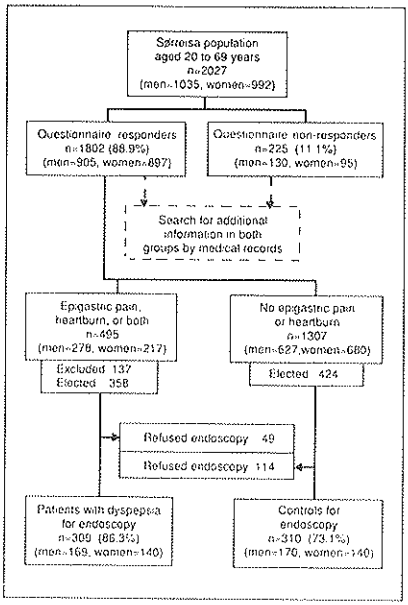
Laboratory of Gastroenterology, Department of Medicine, N-9012 University Hospital of Tromsø, Norway
B Bernersen
P G Burhol
T G Jenssen

Institute of Community Medicine, N-9001 University of Tromsø, Norway
R Johnsen
B Straume

Local Health Office of Sørreisa, N-9310 Sørreisa, Norway
P A Stakkevold

Correspondence to:
Dr R Johnsen, Institute of Community Medicine, Box 417, N-9001 Tromsø, Norway.

Accepted for publication



Flowchart of Sørreisa gastrointestinal disorders study

Biopsy specimens were taken from both the greater and lesser curvatures of the corpus and antrum of the stomach, from the proximal and distal parts of the duodenum, and also from all lesions. The specimens for histological examination were prepared and interpreted by the Department of Histopathology at the University Hospital of Tromsø. Finally, the medical records for the total population were examined for evidence of previously diagnosed peptic ulcers confirmed by barium studies or endoscopy.

Table I shows the distribution of the total population and subpopulations by sex and 10 year age groups. Differences in sex and age distribution between the total population and the subpopulations were evaluated by the χ^2 test.[14]

Population estimates of point prevalences of peptic ulcer were calculated from the gastroscopic findings adjusted for sex and age by analysis of covariance.[15] In this calculation the prevalence rates of controls were used for the non-responder group. The overall prevalences in the total population are based on these population estimates and the figures from the record verification procedure.

TABLE I *Sex-specific percentage age distribution of total population, questionnaire responders and non-responders, subjects endoscoped and subjects refusing endoscopy (Sørreisa 1987)*

	Total population		*Questionnaire responders*		*Subjects endoscoped*		*Questionnaire non-responders*		*Subjects refusing endoscopy*	
	Men	*Women*	*Men*	*Women*	*Men*	*Women*	*Men*	*Women*	*Men*	*Women*
No	1035	992	905	897	339	280	130	95	72	91
Age (yrs):										
20–29	27·1	23·8	26·0	21·7	20·9	18·9	34·6	43·2	31·9	34·1
30–39	22·5	23·9	22·1	24·7	26·5	30·0	25·4	15·8	22·2	31·9
40–49	21·5	20·5	22·4	21·1	31·6	25·4	15·4	14·7	27·8	23·1
50–59	14·0	14·1	14·7	14·4	13·9	15·7	9·2	11·6	12·5	8·8
60–69	14·9	17·7	14·8	18·1	7·1	10·0	15·4	14·7	5·6	2·2
					**	*		*		**

Significant differences in distribution of age compared with total population by χ^2.
*p≤0·01; **p≤0·001.

TABLE II *Sex specific prevalences of self-reported and re verified gastric, duodenal, and peptic ulcer in 1035 men a 992 women aged 20–69 (Sørreisa 1987)*

	Men			*Women*		
	No	*%*	*(No)*	*No*	*%*	*(*
Reported peptic ulcers	59	6·5	(905)	30	3·3	((
Not confirmed by records	9	15·3	(59)	6	20·0	(
Verified peptic ulcers	50		(905)	24		((
False negatives	11	1·3	(846)	2	0·2	((
Ulcers among non-responders	3		(130)	1		(
Total peptic ulcers:	64	6·2	(1035)	27	2·7	((
Gastric ulcer	14	1·4		11	1·1	
Duodenal ulcer	45	4·4		14	1·4	
Combined ulcers	3			2		
Unknown location	2			..		

Confidence intervals based on the Poiss distribution are given when presenting the p valences of ulcers in the total population. Th intervals indicate the random variation due to t sampling fractions of subjects with and witho dyspepsia in the Sørreisa population only. Th only the point estimates apply to a univer population.

The study was approved by the local ethi review board.

Results

Some 1802 of 2027 (88·9%) people returned th questionnaire (Figure). One hundred and thi seven of 495 subjects with dyspepsia w excluded because of an earlier diagnosis of pep ulcer in 89, coronary heart disease in 33, a gall stones or kidney stones in 15. Three hundr and nine of the 358 subjects left were eligible endoscopy, and 309 attended for examinati together with 310 of the 424 matched contro Therefore 79·2% of those invited to endosco participated. Of the 163 refusers, 114 w controls.

There were no significant differences in t sex distribution within the populations (Table Compared with the total population, midd aged men and women were slightly ov represented among those undergoing end scopy. Female non-responders and refusers endoscopy were significantly younger wh compared with the total population. The me age of subjects with dyspepsia was 40·9 yea (range: 20–69) and that of controls was 40·5 yea (range: 20–68).

The results from examination of the medic records are presented in Table II. No medic records were found for 103 of the subjec (5·1%), 12 of whom belonged to the endoscope population without peptic ulcer. Medic records were found for all those who reported previous peptic ulcer, and they showed a fal positive rate of reporting of 15·3% in men a 20·0% in women. Corresponding false negati rates of reporting were 1·3% and 0·2%, respec ively. When four subjects with peptic ulce were included among the non-responders, t lifetime prevalences of peptic ulcer were 6·2% men and 2·7% in women, giving a male:fema ratio of 2·3:1 and a duodenal:gastric ulcer ratio 3·2:1 and 1·3:1 for men and women respectivel

Table III shows endoscopy results in bo subjects with dyspepsia and control subject The presented prevalences are adjusted for ag

TABLE III *Observed numbers and prevalences (%) of gastric ulcer (GU), duodenal ulcer (DU), total peptic ulcer (PU), and deformed duodenal bulb (DDB) found by endoscopy in 339 men and 280 women, aged 20–69 years. Calculated numbers (X) of peptic ulcers for the respective total populations are presented in brackets (Sørreisa 1987)*

	Epigastric pain and/or heartburn						*No epigastric pain or heartburn*					
	Men (n=169)			*Women (n=140)*			*Men (n=170)*			*Women (n=140)*		
	No	*%*	*X*	*No*	*%*	*X*	*No*	*%*	*X*	*No*	*%*	*X*
GU	3	1·8	(4)	2	1·4	(3)	0	–	(–)	1	0·7	(6)
DU	3	1·8	(4)	4	2·9	(6)	1	0·6	(5)	1	0·7	(6)
PU	6	3·6	(8)	6	4·3	(9)	1	0·6	(5)	2	1·4	(10)
DDB	10	5·9	(14)	9	6·5	(13)	4	2·4	(18)	6	4·7	(35)

Prevalences (%) adjusted for age distribution in the local population.

distribution in the total population. Except for gastric ulcers in subjects with dyspepsia, we found higher point prevalences for peptic ulcers and deformed duodenal bulbs in women. The mean age of subjects with peptic ulcers was 45·8 years for men and 45·6 years for women. In the calculation of the number of expected peptic ulcers in the total population, we used the age adjusted prevalences for each ulcer localisation, total peptic ulcers, and deformed duodenal bulbs separately. Because of this the sum of the gastric and duodenal ulcers does not always correspond with the total number of peptic ulcers. Using age adjusted prevalences rather than the corresponding crude prevalences increased the number of peptic ulcers by one in both sexes and the number of deformed duodenal bulbs by one in men and two in women. The male:female ratio for calculated total peptic ulcer then became 0·7:1, irrespective of whether deformed duodenal bulbs were included or not. The duodenal: gastric ulcer ratio was 2·3:1 in men, and 1·3:1 in women.

Table IV gives the overall prevalences in the total population. The 95% confidence limits, using the Poisson distribution, represent the estimated intervals of prevalence in any population comparable with that of Sørreisa. The prevalence of 7·4% for peptic ulcer in men was significantly higher than that for women (4·6%). When deformed duodenal bulbs were included in the peptic ulcer group, however, this difference disappeared, giving an overall prevalence of 10·5% in men and of 9·5% in women.

Discussion

This study was carried out in a well defined population and attracted a high response rate. The study also included blind endoscopy of all subjects with dyspepsia who agreed to the examination as well as of matched healthy controls. In addition we included a search for previously diagnosed peptic ulcers in the local medical records of all subjects who received a questionnaire. The study was designed to eliminate some of the major methodological problems inherent in most prevalence studies on peptic ulcer. To our knowledge, no previous study on peptic ulcer prevalence has used a similar design. Our main findings of a high overall prevalence, a sex ratio close to one, a somewhat unexpected duodenal:gastric ulcer ratio, and a high prevalence of asymptomatic ulcers may mainly be ascribed to our study design.

Lifetime prevalences for peptic ulcer in previous surveys vary from 5·2 to 9·0% in men and 1·9 to 6·0% in women.[5 11 16–19] Necropsy studies, on the other hand, have shown considerably higher prevalences, varying from 18·4 to 20·9% in men and from 9·5 to 14·7% in women.[12 20] Unfortunately, the occurrence of peptic ulcer caused by terminal illnesses is unknown, and since most necropsy populations are highly selected, any comparison with prevalence studies on healthy subjects is questionable.

Our estimated overall prevalences of peptic ulcer disease of 10·5% in men and 9·5% in women are higher than those previously reported for men and even more so for women.

Most prevalence and incidence studies of peptic ulcer have been in patient populations where selection is biased by both the patient's and the doctor's decisions. Even in population based studies,[5 11] the diagnostic procedures have mainly included subjects with severe symptoms, thereby excluding those with minor or no complaints. We have avoided these biases by offering endoscopy to all subjects with dyspepsia together with healthy matched control subjects.

Most surveys have reported that peptic ulcer disease is two to four times more frequent in men than in women,[5 11 21] but the male:female ratio varies both with age and ulcer location. It may thus approach a 1:1 ratio according to Kurata,[1] and also to Doll and Banke in those above 55 years of age.[5 11] In a follow up study of 174 patients with non-ulcer dyspepsia, Krag found that 39% of the men and 42% of the women subsequently developed a peptic ulcer.[22] The male:female ratio of 0·7:1 in the estimated point prevalences of peptic ulcers contrasts with both the corresponding ratio of previously diagnosed peptic ulcers in this population and with those reported in other studies.[5 11 21] The number of peptic ulcers found by endoscopy was small, but the same sex distribution was found among the considerably larger number of deformed duodenal bulbs. These findings indicate that peptic ulcer has been underdiagnosed in women in our population, and this may also be the case in other studies on patient populations. This could partly be due to asymptomatic ulcers, but even among the subjects with dyspepsia, women had more peptic ulcers. The idea that peptic ulcer is mainly a male disease may have led to a higher diagnostic intensity in men.

In the USA and Europe, duodenal ulcer usually occurs at least twice as frequently as

TABLE IV *Estimated* overall prevalences (and 95% confidence intervals† of gastric ulcer, duodenal ulcer, and peptic ulcer exclusive and inclusive of deformed duodenal bulb (DDB) in 1035 men and 992 women aged 20–69 years (Sørreisa 1987)*

	Men (n=1035)		*Women (n=992)*	
	%	*CI*	*%*	*CI*
Gastric ulcer	1·7	(1·6–2·1)	2·0	(1·5–2·6)
Duodenal ulcer	5·2	(4·7–5·8)	2·6	(2·0–3·3)
Peptic ulcer‡	7·4	(6·9–8·2)	4·6	(3·8–5·5)
Peptic ulcer inclusive of DDB‡	10·5	(9·3–11·9)	9·5	(7·9–11·2)

*Combined figures from the endoscopy study and the record verification procedure.
†Based on Poisson distribution.
‡Including ulcers with combined and unknown location.

gastric ulcer.[10 18 21 23] Previous studies in northern Norway have shown higher prevalences and incidences of gastric than duodenal ulcer.[6 8] In southern Norway, on the other hand, Knutsen and Selvaag found a duodenal:gastric ulcer ratio of 1·85:1.[9] In Denmark, incidence rates in patient populations are some four times higher for duodenal (0·13%) than gastric ulcer (0·03%).[10]

One Norwegian study concluded that gastric ulcer relapses are often asymptomatic,[12] but to our knowledge there are no published studies on prevalences of asymptomatic peptic ulcer. Point prevalences of 1·0% for peptic ulcers and 3·2% for deformed duodenal bulb among controls in this study indicate that asymptomatic peptic ulcers are common.

In our estimation of the overall prevalences we have treated those who did not respond to our questionnaire as control subjects. An alternative estimation, where the non-responders were given the point prevalence of subjects with dyspepsia, left the overall prevalence almost unchanged.

All but 12 primary health records of those who underwent endoscopy were found and examined. No information on previous peptic ulcer was found, corresponding with the answers in the questionnaire. This indicates that the peptic ulcers found by endoscopy were first time peptic ulcers.

Despite the comprehensive design of this study, we still cannot account for several potential methodological problems. The unknown rate of scars from previous peptic ulcers and the unknown duration and incidences of asymptomatic and barely symptomatic peptic ulcers represent our major sources of uncertainty. All of these areas of insufficient knowledge with their corresponding flaws in almost any study design probably lead to a considerable underestimation of the true prevalence of peptic ulcer.

In conclusion, we claim that asymptomatic peptic ulcers are quite common, and even that the high overall prevalences found in this study must be regarded as minimum figures. Fina we question the current opinion on the sex r of peptic ulcer disease.

1 Weir RD, Backett EM. Studies of the epidemiology of p ulcer in a rural community: prevalence and natural histo dyspepsia and peptic ulcer. *Gut* 1968; **9**: 75–83.

2 Langman MJS. Changing patterns in the epidemiolo peptic ulcer. *Clin Gastroenterol* 1973; **2**: 219–26.

3 Sonnenberg A. Geographic and temporal variations i occurrence of peptic ulcer disease. *Scand J Gastroe* 1985; **20** (suppl 110): 11–24.

4 Kurata JH, Haile BM, Elashoff JD. Sex differences in p ulcer disease. *Gastroenterology* 1985; **88**: 96–100.

5 Doll R, Jones FA, Buckatzsch MM. *Occupational factors aetiology of gastric and duodenal ulcers.* Medical Rese Council. Report no 276. London: MSO, 1951.

6 Poppe E. Localization of peptic ulcer in a series of from Troms and Tromsø hospital, Norway. *Tidsskr Laegeforen* 1945; **30**: 1063–5.

7 Schanke K. The behavior of gastric and duodenal ulce fishing district in the north of Norway. Studies on frequency and localisation of gastroduodenal ulcer. *Chir Scand* 1946; **suppl 115**: 94.

8 Østensen H, Gudmundsen TE, Bolz KD, Burhol Bonnevie O. The incidence of gastric ulcer and duo ulcer in North Norway. A prospective epidemiolo study. *Scand J Gastroenterol* 1985; **20**: 189–92

9 Knutsen B, Selvaag O. The incidence of peptic ulcer investigation of the population of the town of Dram *Acta Med Scand* 1947; **196**: 341–60

10 Bonnevie O. *Epidemiologiske studier af gastroduodenale ul incidens, kombination og forløb.* (SN). København, 1979

11 Banke L. *Ulcussygdommens epidemiologi.* Københ Århus-Odense: F. A. D. L.'s forlag, 1975

12 Lindstrom CG. Gastric and duodenal peptic ulcer disease well-defined population. *Scand J Gastroenterol* 1978; 139–43.

13 Jorde R, Bostad L, Burhol PG. Asymptomatic gastric ulc follow-up study in patients with previous gastric disease. *Lancet* 1986; **i**: 119–21.

14 Fleiss JL. *Statistical methods for rates and proportions.* York: Wiley-Interscience, 1973.

15 Nie HH, Hull CH, Jenkins JG, Steinbrenner K, Bent SPSS. *Statistical package for the social sciences.* 2nd ed. York: McGraw Hill Inc, 1975

16 Jones FA. Social aspects of peptic ulcer. *J R Inst Publ H* 1955; **18**: 64–74.

17 Almy TP. Prevalence and significance of digestive disea conference. *Gastroenterology* 1975; **68**: 1351–71

18 Monson RR, MacMahon B. Peptic ulcer in Massachu physicians. *N Engl J Med* 1969; **28**: 11–5.

19 Johnsen R, Straume B, Forde OH. Peptic ulcer and non- dyspepsia – a disease and a disorder. *Scand J Prim H Care* 1988; **6**: 239–43.

20 Watkinson G. The incidence of chronic peptic ulcer fou necropsy. *Gut* 1960; **1**: 14–31

21 Pulvertaft CN. Peptic ulcer in town and country. *Br J Prev Med* 1959; **13**: 131–8.

22 Krag E. Pseudo-ulcer and true peptic ulcer. A clin radiographic and statistical follow-up study. *Acta Med S* 1965; **178**: 713–28.

23 Kurata JH, Honda GD, Frankl H. Hospitalization mortality rates for peptic ulcers: a comparison of a H HMO and US data. *Gastroenterology* 1982; **83**: 1008–16

PAPER II

Non-ulcer dyspepsia and peptic ulcer: the distribution in a population and their relation to risk factors

The Sorreisa gastro-intestinal disorder study.
B Bernersen, R Johnsen, B Straume

Abstract

***Background*—The aetiology of non-ulcer dyspepsia and a possible connection to peptic ulcer disease is debated. This paper discusses this problem in a population based study.**

***Aims*—The relation between non-ulcer dyspepsia and peptic ulcer disease was explored by the distribution in the general population and their associations to demographic, lifestyle, and psychological factors.**

***Methods*—All inhabitants of a community aged 20–69 years received a questionnaire concerning abdominal complaints, health, lifestyle, diet, and social conditions. Reports on peptic ulcer were verified with medical records. Dyspeptic subjects and matched healthy, non-dyspeptic controls were endoscoped in a blinded procedure.**

***Subjects*—Of 2027 persons invited, 1802 (88·9%) returned the questionnaire from which dyspeptic subjects and controls were identified. Of 782 subjects invited to endoscopy, 309 dyspeptic and 310 control subjects (79·2%), participated.**

***Results*—Men reported dyspepsia (30·4%) and peptic ulcer (8·7%) more often than women (24·1% and 5·2%, respectively). Non-ulcer dyspepsia was frequent (between 10·6% and 17·2%) in both sexes and age groups up to 60 years, with a lower frequency in both men and women above this age (3·0% and 6·8%). Non-ulcer dyspepsia was associated with having a family history of dyspepsia and of peptic ulcer and the use of tranquillisers. Nearly one third of dyspeptic persons above the age of 40 years had peptic ulcer, but peptic ulcer prevalence was low under this age. Peptic ulcer was associated with a family history of peptic ulcer, smoking, and daily life stress, and also with poor living conditions during childhood, frequent recurrence of herpes labialis, conditions that were associated with *Helicobacter pylori* infection.**

***Conclusions*—Non-ulcer dyspepsia and peptic ulcer have different patterns of relations to lifestyle, social, and psychological factors. The results perhaps support the hypothesis of peptic ulcer being an infectious disease in contrast with non-ulcer dyspepsia.**

(*Gut* 1996; 38: 822–825)

Keywords: dyspepsia, peptic ulcer, population study, *Helicobacter pylori*, lifestyle.

Institute of Clinical Medicine
B Bernersen

and Institute of Community Medicine
B Johnsen
B Straume

University of Tromso, Norway

Correspondence to
Dr R Johnsen, Institute of Community Medicine, MH-University of Tromso, 9037 Tromso, Norway

Accepted for publication
29 December 1995

It is usual that about one third of dyspeptic patients claim to have peptic ulcer disease. The frequency of 'unexplained' dyspepsia depends, however, on the selection of patients. While Gregory *et al* found that only three of 102 dyspeptic patients in general practice developed a peptic ulcer,[1] Kraigh found this in 40% of hospitalised patients.[2]

One study on peptic ulcer disease and non-ulcer dyspepsia in a large population[3] has shown that these conditions had substantially different relations to psychological, social, lifestyle, and dietary variables. Peptic ulcer was strongly associated with age, a family history of peptic ulcer, body mass index, and smoking, whereas non-ulcer dyspepsia was associated with psychological factors and social conditions. In this large population study, however, the diagnoses were not verified. A population based case control study of risk factors in prepylorie and duodenal ulcer patients and controls gave no support to the concept that peptic ulcer disease is a disorder related to psychological stress.[4]

Are peptic ulcer disease and non-ulcer dyspepsia, despite similar symptoms, aetiologically and pathogenetically different conditions? To elucidate the relation between non-ulcer dyspepsia and peptic ulcer disease, we have studied their distribution in a general population and their associations to possible aetiological factors.

Methods

From March to May 1987 all inhabitants of the municipality of Sorreisa in northern Norway aged 20 to 69 years, 2027 men and women, received a postal questionnaire with questions concerning abdominal complaints, health, lifestyle, diet, and social conditions. Of 2027 persons invited, 1802 (88·9%) returned the questionnaire. The inhabitants of this municipality have all their medical contacts with one of the two family physicians at the one and only local health service centre, and their hospital services from the one and only regional hospital. All reports of a previously diagnosed peptic ulcer, were verified by searching individual medical records, which were easily identified in the local health service centre or at the regional hospital.

All subjects giving affirming answers to the first two or the last of the following questions were considered dyspeptic patients: 'Have you ever had abdominal pain of at least two weeks' duration?'; 'If yes, was the pain located to the upper abdomen?' and 'Have you ever had

TABLE I *Prevalences (%) of reported epigastric pain and heartburn (dyspepsia), diagnosed non-ulcer dyspepsia, and verified peptic ulcer according to 10 year age groups and sex. Sorreisa 1987*

	Number		*Dyspepsia (n=409)*		*Non-ulcer dyspepsia (n=233)*		*Peptic ulcer (n=136)*	
Age group	*M*	*F*	*M*	*F*	*M*	*F*	*M*	*F*
20–29	235	195	20·4	19·5	10·6	13·3	3·0	1·0
30–39	200	222	29·0	27·9	15·0	15·3	4·0	4·1
40–49	203	189	40·9	25·4	17·2	15·9	14·8	4·2
50–59	133	129	33·8	24·8	13·5	15·5	12·8	10·9
60–69	134	162	31·3	22·8	3·0	6·8	12·7	8·6
Total	905	897	30·1	24·1	12·4	13·5	8·7	5·2

heartburn or acid regurgitation almost daily during at least one week?[7].

Of 495 dyspeptic persons, 89 subjects reporting a prior history of peptic ulcer, 15 subjects reporting gall stones or kidney stones, and 33 reporting coronary heart disease, were all excluded. The remaining 358 persons were offered an endoscopy free of charge but without any reward. Healthy, non-dyspeptic controls matched for sex and age within the same 10 year age group, were randomly selected and offered an endoscopy as well. The controls were selected from the questionnaire survey, as they reported that they never had experienced abdominal pain at any location or heartburn or acid regurgitation and that they never had consulted their general practitioner with dyspepsia. Of 782 subjects invited to endoscopy, 619 (79·2%) attended, of whom 309 were dyspeptic subjects and 310 controls. All subjects were endoscoped within one month after returning the questionnaire. After completing the verification procedure searching all local medical records for confirmation of a previous peptic ulcer and after endoscoping the 619 persons, 409 persons, of the initial 495 persons, reporting dyspepsia were without a previous or present peptic ulcer. A detailed description of the methods has been published elsewhere.[5] The study was approved by the Regional Committee for Medical Research Ethics.

Endoscopy study

All endoscopies were performed by one of the authors (BB), who is a trained endoscopist. The endoscopist was masked to whether he examined a dyspeptic or a non-dyspeptic person. A gastric or duodenal ulcer was diagnosed if an ulceration greater than 0·5 cm was seen proximally or distally to the pylorus, respectively. Deformity of the duodenal bulb was considered to be present when flattening, scars, stenosis, or narrowing of the bulb was seen. Endoscopic duodenitis was diagnosed according to the criteria of Venables.[6]

Biopsy specimens for histological diagnosis were taken from all lesions. Stomach biopsy specimens for *Helicobacter pylori* cultures, were placed in 0·5 ml of glucose/saline solution (25% glucose in 0·9% saline solution), ground, and dispersed on blood agar and on brain-heart infusion agar containing horse (5% v/v) blood within five minutes after endoscopy.[7]

Definition of groups for analysis

Dyspeptic group – All persons with dyspep as defined above, but without a present or p vious peptic ulcer.

Non-ulcer dyspepsia – All dyspeptic subje attending the endoscopic study without peptic ulcer, deformity of the duodenal bulb endoscopic duodenitis of the duodenal bu

Peptic ulcer – All persons with peptic ulc verified with any of the medical records and persons having a peptic ulcer or an ulcer s (deformed duodenal bulb) at the endosco

Reference population – In the logistic regr sion analysis of dyspepsia, non-ulcer dyspep and peptic ulcer, the reference populati comprised subjects without any of the m tioned conditions.

Regression analyses

The following independent variables w explored and finally assessed in a logis regression: age; sex; daily smoking (yes/n number of cigarettes smoked daily; previ smoking (yes/no); coffee consumption (no or less than 1 cup a day, 1–5 cups, and 6 c or more a day); beer, wine and liquor c sumption (graded 0–2); nourishment as b (mother's milk or not); regularity of me excessive use of spices, ketchup or musta use of some specific drugs (aspirin, n steroidal anti-inflammatory drugs, sleepi pills and tranquillisers), shift work (all yes/n social stress (four categories, never to all time); physical activity at leisure time (grad 1–4: sedentary, moderate, active, and h training); living conditions during childho (four categories, from very difficult to v good), and dyspepsia or peptic ulcer, or bo in the family (first degree relatives); bother by herpes labialis (four categories, never frequent); reporting complaints as frequ headache, unspecific vertigo, palpitations a insomnia, where reporting more or less th two of these symptoms, respectively, w graded as yes/no.

Statistical methods

Age trends were tested by Mantel-Haenszel test. Logistic regression and adjustment for a and sex distribution by analysis of covarian were made in the SPSSX statistical progra

Results

Table I shows the prevalences of reported d pepsia, non-ulcer dyspepsia, and peptic ulc Of the 309 persons with dyspepsia end scoped, 31 had a peptic ulcer or a deform duodenal bulb at the present time and 45 h an endoscopic duodenitis, leaving 233 perso with non-ulcer dyspepsia.

There were no significant differences in fr quency of dyspepsia between the two sex when stratified for age, but there was a sligh increasing trend with age in the frequency dyspepsia in men ($p=0·003$). The prevalen of non-ulcer dyspepsia did not differ betwe the sexes and seemed stable throughout t

age span, only showing a pronounced decrease in the age group above 60 years. Peptic ulcer had a significant sex difference with more diagnosed peptic ulcers in men ($p=0{\cdot}002$) and an increasing prevalence with age for both sexes ($p<0{\cdot}0001$) with a pronounced increase in men aged over 40 years and women aged over 50 years.

Table II shows the results of the regression analysis. A corresponding analysis of dyspepsia excluding persons reporting irritable bowel symptoms according to Manning's criteria,[8] gave mainly the same results as presented for dyspepsia. The non-ulcer dyspepsia group, consisting of the subjects with dyspepsia in the endoscopy population when excluding organic pathological endoscopic findings, had chiefly the same relations as the dyspepsia group, but in addition showed a significant association with use of tranquillisers. The analysis of non-ulcer dyspepsia contrasted with the matched controls gave the same relations (with a somewhat lower strength).

Finally, in persons with peptic ulcer disease, there were significant contributions from age, sex, family history of peptic ulcer, smoking, previous smoking, tea drinking, frequent recurrences of herpes labialis, breast fed as a baby, poor living conditions during childhood, and the feeling of lack of time.

In an analysis of the endoscoped persons, *H pylori* infection was found in 49·6% of subjects having frequent recurrences of herpes labialis, while subjects never or seldom having this condition were infected in 39·7% ($p=0{\cdot}04$). Subjects having poor living conditions during their childhood were infected with *H pylori* in 49·6%, while subjects having good or fair living conditions during their childhood had this infection in 37·5% ($p=0{\cdot}003$).

Discussion

Dyspepsia is a common disorder, even when symptoms are restricted to upper abdominal pain and heartburn or acid regurgitation of at least two weeks' duration as in this study. We found that men were more likely to be afflicted with dyspepsia, with a small increase with age, unlike women. Non-ulcer dyspepsia occurred with a similar frequency in both sexes up to 60 years, but was less common in older people of both sexes. Peptic ulcer was seldom found up to the age of 40 years in men and 50 years in women, but in older dyspeptic patients nearly one third had a peptic ulcer.

Dyspepsia has been defined and classified in various ways,[9 11] but in this study the definition includes the most commonly accepted symptoms with a low grade of selection on severity and duration. In our definition of non-ulcer dyspepsia, we have chosen to exclude both peptic ulcer, ulcer scars (deformity), and endoscopic duodenitis of the duodenal bulb.[12]

Our investigation shows that relations to background factors were quite similar for dyspepsia and non-ulcer dyspepsia, the only difference was that patients with non-ulcer dyspepsia, were treated, for example with reduction of coffee drinking and use of tranquillisers. In epidemiological studies there are few reasons to differentiate between dyspepsia and non-ulcer dyspepsia.

Non-ulcer dyspepsia was associated with a family history of peptic ulcer and also with a family history of dyspepsia. To our knowledge, there are no theories of inheritance of dyspepsia, but dyspeptic symptoms may be inherited by learning habits and how to report them.[13] Our finding of a relation to previous smoking in dyspeptic subjects similar to the association between peptic ulcer and tea drinking, may be seen as a result of changed habits related to the disease.[14] We know of no previous reports on associations between tea drinking and peptic ulcer and this finding may be a spurious one or show changed habits among peptic ulcer patients because of medical counselling. Tea drinkers controlled for earlier coffee drinking showed that 38% of dyspeptic subjects and 21% of non-dyspeptic subjects had stopped coffee drinking.

Peptic ulcer has in this study a quite different pattern of relations, firstly to age and sex, but also to well known factors as smoking and a family history of peptic ulcer. For peptic ulcer this last relation may fit in with theories of inheritance,[15] but also with family clustering of *H pylori*.[16] The relations to frequent recurrences of herpes labialis may indicate a connection to infectious diseases. We found an association between frequent herpes labialis recurrences and *H pylori* infection. Duodenal ulcer has earlier been connected to herpes virus

TABLE II—*Odds ratio (OR) of the independent variables in a logistic regression analysis among 1802 men and women with dyspepsia (n=409), non-ulcer dyspepsia (n=233), and peptic ulcer (n=126) in contrast with the reference population (n=1267). Sørreisa 1987*

	Dyspepsia (n=1676)		*Non-ulcer dyspepsia (n=1500)*		*Peptic ulcer (n=1393)*	
Independent variable	*OR*	*CI**	*OR*	*CI**	*OR*	*CI**
10 Year age group	1·02	0·93 to 1·13	0·90	0·80 to 1·01	1·50	1·28 to 1·76
Sex (female=0, male=1)	1·53	1·19 to 1·96	0·85	0·63 to 1·15	1·90	1·24 to 2·90
Family history of dyspepsia (no/yes)	2·21	1·71 to 2·84	2·20	1·62 to 2·98	1·54	0·94 to 2·40
Peptic ulcer in the family (no/yes)	1·83	1·41 to 2·37	1·87	1·36 to 2·58	2·50	1·65 to 3·77
Smoking (no/yes)	1·69	1·27 to 2·26	1·46	1·03 to 2·06	3·53	2·08 to 5·98
Previous smoking (no/yes)	1·98	1·43 to 2·73	1·58	1·06 to 2·34	2·08	1·16 to 3·73
Tea drinking (no/yes)	1·15	0·89 to 1·49	1·16	0·85 to 1·60	2·11	1·59 to 3·67
Frequent herpes labialis (no/yes)	1·40	1·05 to 1·85	1·27	0·90 to 1·81	2·13	1·36 to 3·35
Breast feeding as baby (no/yes)	0·97	0·77 to 1·23	1·29	0·96 to 1·74	1·53	1·01 to 2·32
Frequent complaints (no/yes)	2·28	1·69 to 3·09	1·68	1·14 to 2·46	1·12	0·65 to 1·93
Use of tranquillisers (no/yes)	1·50	0·83 to 2·70	2·07	1·07 to 4·01	0·84	0·32 to 2·20
Feeling of lack of time (no/yes)	1·06	0·78 to 1·43	1·25	0·88 to 1·78	1·67	1·03 to 2·69
Poor living conditions during childhood (no/yes)	1·15	0·89 to 1·49	1·22	0·89 to 1·67	1·88	1·25 to 2·82

*CI=95% confidence intervals.

infection and a theory proposing that duodenal ulcer could be of herpetic origin.[17,18] We did not expect that being breast fed as baby would be associated with peptic ulcer. We found no relation between *H pylori* infection and breast feeding as baby in this study and to our knowledge no data connecting these conditions exist. The relation is weak, and this finding should be interpreted with caution. Poor living conditions during childhood have been connected with low resistance against other diseases,[19] but may also be connected with early infection of *H pylori*.[20] In our endoscopy group subjects with poor living conditions during their childhood had *H pylori* infection significantly more often than those better off during their childhood. It may be hypothesised from these data that several putative risk factors for peptic ulcer are spurious and express an association with infective agents as *H pylori*.

Regardless of the different pattern of relations to background factors between peptic ulcer and dyspepsia, the clinician will always ask when dyspepsia represents peptic ulcer or not. It would be financially worthwhile to carry out an endoscopy or a breath test diagnosing *H pylori* infection. In our population study, the *H pylori* status was obtained in all persons who had an endoscopy, dyspeptic as well as non-dyspeptic controls.[7] From these data it is obvious that a positive *H pylori* diagnosis could not tell us whether a dyspeptic person has a peptic ulcer or not. The question is whether or not the non-ulcerous mucosa will help the practitioner to decide what advice and what treatment to give. At least, the low occurrence of peptic ulcer among young people support a reluctant attitude towards endoscopy of young dyspeptic patients.

The results in this study may be questioned because of the comparatively small numbers for all groups studied. The cross sectional design does not allow us to make conclusive inferences on causality. Furthermore, we do not have data on the *H pylori* occurrence in our total study group, only in the 619 subjects endoscoped. These disadvantages may to some extent be compensated by our comprehensive investigations to verify reported ulcers as most studies on peptic ulcer in studies with larger numbers are burdened with diagnostic problems.[21] The 'blinding' of the endoscopy of all dyspeptic subjects and controls will also red the possibility of biased findings.

We conclude that non-ulcer dyspepsia peptic ulcer have different patterns of relati to lifestyle, social, and psychological facto The results of this study seem, with so reservations, to support the hypothesis of p tic ulcer being an infectious disease in contr with non-ulcer dyspepsia.

1 Gregory DW, Davies GT, Evans KT, Rhodes J. Natural tory of patients with X-ray-negative dyspepsia in ge practice. *BMJ* 1972; 4: 519–20.

2 Krogh B. Pseudo-ulcer and true peptic ulcer. A clin radiographic and statistical follow-up study. *Acta Scand* 1965; 178: 713–28.3.

3 Johnsen R, Straume B, Forde OH. Peptic ulcer and ulcer dyspepsia – a disease and a disorder. *Scand J Health Care* 1988; 6: 239–43.

4 Adami HO, Bergström R, Nyrén O, Forhaug K, Gustav S, Lood L, *et al*. Is duodenal ulcer really a psychosom disease? A population-based case-control study. *Scan Gastroenterol* 1987; 22: 889–96

5 Bernersen B, Johnsen R, Straume B, Burhol PG, Jen TG, Stalsberg PA. Towards a true prevalence of pe ulcer: the Sarpsa gastrointestinal disorder study 1990; 31: 989–92.

6 Venables CW. Duodenitis. *Scand J Gastroenterol* 1985 (suppl 109): 91–7

7 Bernersen B, Johnsen R, Bostad L, Straume B, Sommer Burhol PG. Is Helicobacter pylori the cause of dyspep *BMJ* 1992; 304: 1276–9.

8 Manning AP, Thompson WG, Heaton KW, Morris Towards positive diagnosis of irritable bowel. *BMJ* 19 2: 653–4.

9 Heatley RV, Rathbone BJ. Dyspepsia: a dilemma doctors? *Lancet* 1987; ii: 779–82

10 Colin-Jones DG. Management of dyspepsia: report working party. *Lancet* 1988; ii: 576–9.

11 Talley NJ, Zinsmeister AR, Schleck CD, Melton II Dyspepsia and dyspepsia subgroups: a population-ba study. *Gastroenterology* 1992; 102: 1259–68

12 Greenstaw R, Sheahan DG, DeLuca V, Miller D, Mye D, Myerson P. Gastroduodenitis: a invader concep peptic ulcer disease. *Dig Dis Sci* 1980; 25: 660–72.

13 Whitehead WE, Winget C, Fedoravicius AS, Woole Blackwell B. Learned illness behavior in patients w irritable bowel syndrome and peptic ulcer. *Dig Dis* 1982; 27: 202–8.

14 Jacobsen BK, Bjelke E, Kvale G, Heuch I. Coffee dr ing, mortality, and cancer incidence: results from Norwegian prospective study. *J Natl Cancer Inst* 19 76; 823–31

15 Anonymous. Duodenal ulcer inheritance [Editorial]. *La* 1979; i: 650–1

16 Odercha G, Vaira D, Holton J, Ansley C, Altare F, Boero *et al*. Helicobacter pylori in children with peptic ulcer their families. *Dig Dis Sci* 1991; 36: 572–6

17 Vestergaard BF, Rune SJ. Type specific herpes simp virus antibodies in patients with recurrent duodenal ul *Lancet* 1980; i: 1273–5

18 Anonymous. Viruses and duodenal ulcer [Editorial]. *La* 1981; i: 705–6

19 Forsdahl A. Are poor living conditions in childhood adolescence an important risk factor for arteriosclero disease? *Br J Prev Soc Med* 1977; 31: 91–5

20 Mendall MA, Goggin PM, Molineaux N, Levy J, Toos Strachan D, *et al*. Childhood living conditions Helicobacter pylori seropositivity in adult life. *La* 1994; 339: 896–7

21 Langman MJS. Changing patterns in the epidemiology peptic ulcer. *Clinics in Gastroenterology* 1973; 2: 219–

PAPER III

PAPERS

Prevalences of endoscopic and histological findings in subjects wit and without dyspepsia

Roar Johnsen, Bjørn Bernersen, Bjørn Straume, Olav Helge Førde, Leif Bostad, Per G Burhol

Abstract

Objective—To examine the association between dyspeptic symptoms and endoscopic and histological diagnoses.

Design—Cross sectional study of people with dyspepsia and controls matched for age and sex identified by questionnaire survey of all inhabitants aged 20 to 69. Endoscopy and histological examination was performed with the examiner blind to whether or not the patient had dyspepsia.

Setting—Population based survey in Sørreisa, Norway.

Subjects—All people with dyspepsia and age and sex matched people without dyspepsia were offered endoscopy. A total of 309 people with dyspepsia and 310 without dyspepsia underwent endoscopy, giving 273 matched pairs.

Main outcome measures—Prevalences of endoscopic and histological diagnoses made according to internationally accepted standards.

Results—In all, 1802 of 2027 (88·9%) people returned the questionnaire. Of the 163 subjects who refused endoscopy, 114 were controls. Of five endoscopic and four histological diagnoses only peptic ulcer disease, endoscopic duodenitis, and active chronic gastritis were diagnosed significantly more often in people with dyspepsia. In all, 30% to 50% of the diagnoses of mucosal inflammation and peptic ulcer disease were made among subjects without dyspepsia, and only 10% of both those with and those without dyspepsia had normal endoscopic findings.

Conclusions—The diagnostic findings, with possible exceptions of peptic ulcer disease and endoscopic duodenitis, showed no association of clinical value with dyspeptic symptoms. The small number of "normal" endoscopic findings in both those with and those without dyspepsia challenge well accepted endoscopic and histological diagnostic criteria with relation to the upper gastrointestinal tract.

University of Tromsø, N-9000 Tromsø, Norway
Roar Johnsen, MD, *research fellow in general practice*
Bjørn Bernersen, MD, *research fellow in gastroenterology*
Bjørn Straume, MD, *assistant professor in epidemiology*
Olav Helge Førde, MD, *professor in health services research*
Leif Bostad, MD, *consultant pathologist*
Per G Burhol, MD, *professor in gastroenterology*

Correspondence to:
Dr Johnsen.

BMJ 1991;302:749-52

Introduction

The disability, suffering, and health care resources associated with patients in whom disease is wrongly suspected represent a mounting burden in modern medicine and permanently challenge our ability to recognise normality and discriminate between disease and "non-disease."

In gastroenterology the controversy around the "dyspeptic myth" of gastroduodenitis is one of many examples of this problem.[1] So far the discussion on gastroduodenitis has mainly focused on the association with dyspepsia and peptic ulcer disease.[2-5] Studies on the occurrence of this condition among people without dyspepsia, which could have settled parts of the controversy, have been scarce and based on small populations.[6-9] The lack of agreement on wh symptoms should be included in the term "dyspeps may likewise have nourished the controversy.

A working party of gastroenterologists defi dyspepsia as any symptom "considered to be refera to the proximal alimentary tract,"[10] while others ha restricted the term to "chronic or recurrent abdomi pain or nausea, or abdominal symptoms, often rela to feeding."[9-11] Any population of people with dyspep selected according to these definitions could v considerably regarding both the character of sin symptoms and that of complexes of symptoms.

Most studies of patient populations with differ prevalences of peptic ulcer disease are inconclus regarding the relation between chronic gastritis a dyspepsia and peptic ulcer disease. The few populat studies on chronic gastritis reject any association w dyspepsia and question an association with peptic ul disease.[12-14] Corresponding surveys on duodenitis not available, and the discussion on whether endosco and histological duodenitis represents the sa disorder and is part of the range of peptic ulcer disea is based on patient surveys and a few studies in heal volunteers.[15-17]

A discussion on normality and the clinical va of dyspeptic symptoms associated with differ conditions in the upper gastrointestinal tract can assessed only from population based studies. Desp common agreement on the diagnostic criteria of stages of different pathological conditions in the up gastrointestinal tract,[18-21] a main problem in all o studies is the observer bias related to the knowledg whether or not the patient has symptoms. To achie non-biased assessment of the clinical value of dyspe symptoms we performed endoscopy in subjects w and without dyspeptic symptoms, with the exam being unaware of whether or not the subjects symptoms.

Methods

After a population based questionnaire survey o inhabitants aged 20-69 years in the municipality Sørreisa in northern Norway (n=2027)[8] all subj reporting dyspepsia and matched subjects with dyspepsia were offered endoscopy of the upper gas intestinal tract. There was no financial gain or hir health benefits associated with the invitation. subjects with dyspepsia were selected on the basi answers to the first two or the last, or both, of the t questions: "Have you ever had abdominal pain least two weeks' duration?"; "If yes, was the located to the upper abdomen?"; and "Have you had heartburn or acid regurgitation almost daily du at least one week?"

Subjects with dyspepsia who reported a histor peptic ulcer, abdominal surgery, gall stones, kid stones, or cardiac disease were excluded. For

without dyspepsia, matched for sex and age within the same 10 year age group, was randomly selected and offered endoscopy. Thus 782 subjects were invited for endoscopy, and 309 subjects with dyspepsia and 310 controls attended (79·2%), giving 273 matched pairs. Details of methods are given elsewhere.[18] All endoscopies were performed by one of us (BB), who is a trained endoscopist and who was blinded with regard to whether he was examining a subject with dyspepsia or a control subject. Endoscopic findings were classified according to the criteria described by Savary and Miller (for oesophagitis),[19] Johnsson *et al* (for hiatus hernia),[20] Myren and Serck-Hanssen (for endoscopic gastritis and gastroduodenal reflux),[21] Venables (for duodenitis),[17] and Bernersen *et al* (for peptic ulcer and deformed duodenal bulb).[18] Peptic ulcer disease was defined as having an active peptic ulcer or a deformed duodenal bulb.

Biopsy specimens were obtained from the corpus and antral part of the stomach, including both the greater and lesser curvatures; from the proximal and distal parts of the duodenum; and from all visible lesions. The specimens for morphological examination were prepared according to standard methods and interpreted blindly by an experienced pathologist (LB). Inflammation of gastric and duodenal mucosa was classified according to Whitehead *et al*[14,15] and Owen.[22] The study was approved by the regional committee of medical research ethics.

Statistics—Differences in overall prevalences were examined by the χ^2 test and by McNemar's test in the paired analysis. Age trends, overall and within sexes, were evaluated by *t* test of the regression coefficients in simple linear regression.[23] All prevalences of various symptoms were adjusted for age and sex in a covariance analysis.[24]

Results

Some 1802 of 2027 (88·9%) subjects returned the questionnaire. Of the 163 subjects who refused endoscopy, 114 were controls. There were no significant differences in the sex distribution between responders and non-responders and between subjects who had endoscopy and those who refused endoscopy. Compared with the total population middle aged men and women were slightly overrepresented among those who had endoscopy. Women who did not respond to the questionnaire or who refused endoscopy were significantly younger compared with the total population.[19]

Figures 1 and 2 present the sex and age specific frequencies of various endoscopic and histological diagnoses and the proportion of subjects with normal mucosa in their biopsy specimens for 339 men and 280 women. The data for subjects with dyspepsia controls were pooled as the age and sex distribution the various diagnoses were generally equal in t groups. The age adjusted frequencies of oesopha found on endoscopy were 13·3% in men and 5·8% women (p=0·002), and the corresponding figures duodenitis were 22·8% and 5·9% (p=0·0001) and peptic ulcer disease were 5·1% and 7·9% (p=0·3) 1). The frequencies of all types of gastritis found histological examination in both sexes and duoden in women showed a significant age trend but significant sex differences (fig 2). No signific differences in age trends between sexes were found any of the diagnoses.

Table I gives the paired analysis of the prevalence

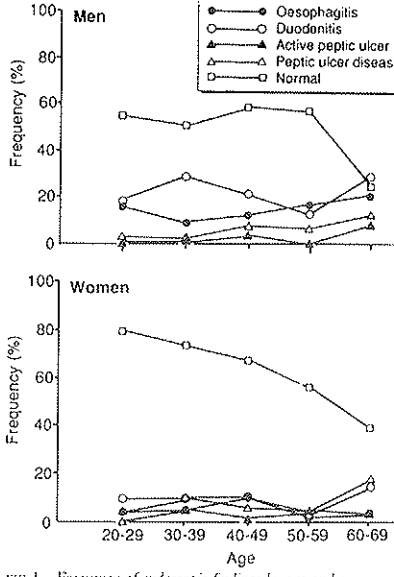


FIG 1—*Frequency of endoscopic findings by age and sex amon men and 280 women in Sørreisa, Norway, in 1987*

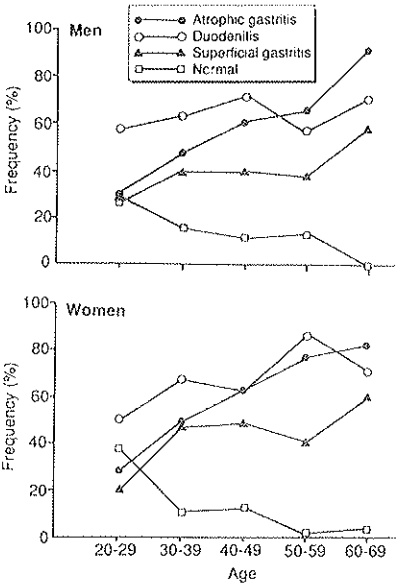


FIG 2—*Frequency of histological findings by age and sex among men and 280 women in Sørreisa, Norway, in 1987*

TABLE I—*Prevalences of endoscopic and histological findings in 273 subjects with dyspepsia and 273 sex and age matched controls in Sørreisa, Norway, in 1987. Figures are numbers (percentages)*

	Subjects with dyspepsia	Controls	Discordant pairs*	Significance† (p Value)
Endoscopic diagnosis				
Oesophagitis (grade I or II)	33 (12·1)	22 (8·1)	31/20	0·26
Hiatus hernia	9 (3·3)	7 (2·6)	8/6	0·79
Superficial gastritis	55 (20·1)	44 (16·1)	48/37	0·28
Atrophic gastritis	10 (3·7)	11 (4·0)	10/11	1·0
Duodenogastric reflux	50 (18·3)	35 (12·8)	41/26	0·09
Peptic ulcer disease	23 (8·4)	10 (3·7)	22/9	0·02
Duodenitis	55 (20·1)	24 (8·8)	52/21	0·0005
Normal endoscopy	146 (53·5)	181 (66·3)	47/82	0·003
Histological diagnosis				
Chronic superficial gastritis	118 (43·2)	102 (37·4)	63/47	0·15
Chronic atrophic gastritis (all types)	170 (62·3)	138 (50·5)	81/49	0·007
Active chronic gastritis	73 (26·7)	52 (19·0)	58/37	0·04
Duodenitis	170 (62·3)	191 (70·0)	38/59	0·04
Normal histology	43 (15·8)	35 (12·8)	37/29	0·4
Normal endoscopy/histology	28 (10·3)	31 (11·4)	26/29	0·8

*Number of discordant pairs in the 2×2 table. †By McNemar's test.

TABLE II—*Age and sex adjusted prevalences of endoscopic and histological findings in subjects reporting dyspepsia and in matching controls in Sørreisa, Norway, in 1987. Figures are numbers (percentages) [95% confidence intervals]*

Diagnosis	Subjects with dyspepsia			Controls (n=310)
	Epigastric pain (n=64)	Heartburn (n=142)	Both epigastric pain and heartburn (n=61)	
Endoscopic diagnosis				
Oesophagitis (grade I or II)	10 (15·8) [7·8 to 26·9]	15 (10·5) [6·1 to 17·1]	7 (11·5) [4·7 to 22·2]	25 (9·0) [5·5 to 12·1]
Peptic ulcer disease	3 (3·8) [1·0 to 13·1]	13 (9·8) [5·1 to 15·4]	8 (12·4) [5·8 to 24·2]	12 (3·8) [2·1 to 6·9]
Duodenitis	9 (14·2) [6·6 to 25·0]	33 (22·9) [16·9 to 31·5]	19 (31·5) [19·9 to 44·3]	30 (9·7) [6·6 to 13·6]
Histological diagnosis				
Superficial gastritis	33 (49·1) [38·7 to 64·3]	63 (46·2) [36·7 to 53·1]	24 (37·4) [27·1 to 52·7]	117 (37·6) [34·4 to 45·7
Chronic atrophic gastritis (all types)	45 (65·4) [57·6 to 81·1]	87 (64·9) [52·8 to 69·5]	35 (53·5) [44·1 to 70·0]	152 (48·7) [44·2 to 55·8
Active chronic gastritis	26 (39·3) [28·5 to 53·6]	30 (22·2) [15·0 to 29·2]	14 (21·8) [13·2 to 35·5]	55 (17·6) [14·1 to 23·2
Duodenitis	44 (67·5) [55·9 to 80·0]	81 (57·0) [49·2 to 66·1]	43 (69·5) [57·4 to 81·5]	212 (68·3) [64·5 to 75·1

diagnoses based on endoscopic and histological findings in the 273 matched pairs of subjects. The only highly significant differences between subjects with dyspepsia and controls were found in subjects with duodenitis on endoscopy ($p=0·0005$) and those with histological findings of chronic atrophic gastritis ($p=0·007$). When subjects with active chronic gastritis were excluded from the analysis the difference between subjects with dyspepsia and controls with respect to histological findings indicating chronic gastritis became insignificant. In fact, 50% of controls had atrophic gastritis. More controls than subjects with dyspepsia had duodenitis on histological examination. The figures for duodenitis grade II (increased cellularity of the lamina propria and abnormality of the surface epithelium) were 20·1% in subjects with dyspepsia and 24·2% in controls.

Of the 309 subjects with dyspepsia, 125 (40·5%) reported having epigastric pain, of whom 64 (51·2%) reported having no simultaneous heartburn, and 245 (79·3%) reported having heartburn or acid regurgitation. Forty two (17%) of those with heartburn or acid regurgitation had abdominal pain that was not in the epigastric region, 142 (58%) had heartburn without abdominal pain, and 61 (24·9%) had both heartburn and epigastric pain.

Table II gives the age and sex adjusted prevalences of the endoscopic and histological findings; the dyspeptic subjects are grouped according to reported symptom. (The 42 subjects with abdominal pain other than epigastric pain were omitted from this analysis.) All diagnoses based on endoscopy showed the highest point estimates among those with both epigastric pain and heartburn, except for oesophagitis, which was at its highest prevalence in the subjects with epigastric pain. The prevalences of peptic ulcer disease and duodenitis were higher among those with heartburn than among those with only abdominal pain, though the confidence intervals overlapped. The prevalences of all gastritis found on histological examination were, on the contrary, highest in the group with epigastric pain. The confidence intervals were, however, wide in all three symptom groups, showing the loss of statistical power due to small numbers.

Discussion

This study was based on a population survey with a high rate of response (88·9%) and was designed to explore the associations between dyspeptic symptoms and endoscopic findings by comparing the findings in subjects with dyspepsia and those in matched controls. To minimise observer bias both the endoscopist and the pathologist were unaware whether or not the subjects had symptoms of dyspepsia, and the pathologist had no information on the endoscopic findings.

Our main observation was that 30% to 50% of the cases of gastroduodenal inflammation and peptic ulcer disease were diagnosed among control subjects and that only 10% of controls were without any endoscop or histological diagnoses. The considerable overlap diagnoses of inflammation between subjects with a subjects without dyspepsia may support, with reserv tions because of our cross sectional design, the Spir hypothesis that mucosal inflammation is a continuu with peptic ulcer disease as a stage in the process.[26] T relation, if any, between the inflammatory process a dyspeptic symptoms is, however, obscure.

Multiple methodological problems are inherent this kind of study. Besides the observer bias proble special care should be devoted to selecting the popu tion to be examined. Compared with subjects population based surveys hospital patients are hig selected regarding age, seriousness of symptoms, a disease. Furthermore, the expected frequencies endoscopic findings could depend, as shown in t study, on which dyspeptic symptoms the selection the population is based. For comparative purposes t wide definition of dyspepsia seems unsuitable.

ASSOCIATION BETWEEN DYSPEPSIA AND DIAGNOSES

The association between dyspepsia and peptic ul disease is well documented and accepted, althou peptic ulcers that do not cause dyspepsia are p valent.[9 16 26] Endoscopic duodenitis, which displays t same clinical picture as peptic ulcer disease, is a associated with dyspepsia, either as a part of the ra of peptic ulcer disease[1 27 28] or as a clinical entity of own.[8 27 29] Although the associations between dyspep and peptic ulcer disease and dyspepsia and endosco duodenitis were confirmed in the present study, 3 of the subjects with these diagnoses did not h dyspepsia.

The association between chronic gastritis dyspeptic symptoms, on the other hand, is disputed many authors,[3 16] though Earlam *et al* and Joffe Rao claim that corpus and antral gastritis could ca symptoms.[10 11] We found that active chronic gastr was significantly commoner among subjects w dyspepsia, but gastritis was diagnosed in more t 50% of the controls, and more than 40% of the case gastritis, with or without activity, were diagno among people without dyspepsia. Neither grade I grade II histologically classified duodenitis was ass ated with dyspepsia. In fact, the point estimate duodenitis was higher among controls than am people with dyspepsia.

NON-DISEASE IN UPPER GASTROINTESTINAL TRACT

Endoscopic examination of subjects with dyspep supplemented with histological diagnosis, has sh that few subjects (12-25%) have a "normal" up gastrointestinal tract.[8 9 12 29 30 31] Two of the stu were, however, concerned only with gastritis.[32 our study the subjects with normal findings w surprisingly few. Some of the endoscopic diagno such as gastritis, duodenogastric reflux, and hi hernia, may be considered non-pathological conditi and such results classified as normal. Still, the h

frequency of abnormalities on histological examination would mean that few subjects had a normal mucosa.

The clinical value of pathological findings depends on their ability to classify subjects with common features—for example, having symptoms—or to give information on prognosis. The endoscopic findings in our study, with the possible exceptions of peptic ulcer disease and endoscopic duodenitis, showed no association with dyspeptic symptoms that was of clinical value. This corresponds well with the results of therapeutic trials that show a beneficial effect both on symptoms and peptic ulcer disease and endoscopic duodenitis[9 14] whereas convincing evidence of a therapeutic effect on other mucosal inflammations is lacking. In the population the degree of mucosal inflammation apparently represents various degrees in an inflammatory process rather than separate diagnostic entities. Traditionally, clinicians have used as a cut off point between no disease and disease the presence of an ulcer in the mucosa. The ulceration process must, however, have an initial stage at which the ulcer is invisible through the endoscope.[15] The location, distribution, and severity of the inflammation might contribute when considering alternative cut off points. In the paired analysis we found no association between symptoms and isolated inflammation in the corpus, antrum, proximal, or distal duodenum. Location and distribution of the inflammation therefore had poor discriminatory power in this study. Although Toukan *et al* have shown that a high neutrophilic cell count could discriminate between symptom causing gastritis and inflammation not causing dyspepsia,[16] we think that the only rational basis for therapeutic considerations is the symptoms, and not endoscopically or histologically diagnosed inflammation of a mild to moderate degree.

The surprisingly high frequency of positive diagnoses in our study cannot be explained by use of odd provincial diagnostic criteria: both endoscopy and histological examination were performed according to internationally accepted and diagnostic standards of widespread use. When, despite this, the proportion of normal findings on standard endoscopy amounts to a modest 10% it reflects the use of a normative concept of normality, where the norm is the non-prevalent, non-inflamed gastrointestinal mucosa. Our findings challenge both endoscopists and pathologists to search for new distinctions between disease and non-disease.

1 Thomson WO, Joffe SN, Robertsen AG, Lee FD, Imrie CW, Blumgart LH. Is duodenitis a dyspeptic myth? *Lancet* 1977;ii:1197-8.
2 Anonymous. Duodenitis—any progress? *Lancet* 1985;ii:1222-3.
3 Cheli R. Symptoms in chronic non-specific duodenitis. *Scand J Gastroenterol* 1982;17 (suppl 79):84-6.
4 Joffe SN. Relevance of duodenitis to non-ulcer dyspepsia and peptic ulceration. *Scand J Gastroenterol* 1982;17 (suppl 79):88-97.
5 DeLuca VA, Winnan GG, Sheahan DG, *et al*. Is gastroduodenitis part of peptic ulcer disease? *J Clin Gastroenterol* 1981;3 (suppl 2):17-22.
6 Talley JN, Phillips SF. Non-ulcer dyspepsia: potential causes and pathophysiology. *Ann Intern Med* 1988;108:865-79.
7 Giuslandi M. Focus on duodenitis. *Dig Dis Sci* 1986;4:231-9.
8 Kreuning J, Bosman FT, Kuiper G, Van Der Wal AM, Lindman J. Gastric and duodenal mucosa in "healthy" individuals. *J Clin Pathol* 1978;31:69-77.
9 Akdamar K, Ertan A, grawal NM, McMahon FG, Ryan J. Upper gastrointestinal endoscopy in normal asymptomatic volunteers. *Gastrointestinal Endoscopy* 1986;32:78-80.
10 Colin-Jones DG. Management of dyspepsia. report of a working party. *Lancet* 1988;ii:576-9.
11 Barbara L, Camilleri M, Corinaldesi R, *et al*. Definition and investigation of dyspepsia. Consensus of an international ad hoc working party. *Dig Dis Sci* 1989;34:1272-6.
12 Siurla M, Varis K, Kekki K. New aspects on epidemiology, genetics and dynamics of chronic gastritis. *Frontiers of Gastrointestinal Research* 1980;6:148-66.
13 Villako K, Ihanaeka T, Tamm A, Tammur R. Upper abdominal complaints and gastritis. *Ann Clin Res* 1984;16:192-4.
14 Whitehead R, Truelove SC, Gear MWL. The histological diagnosis of chronic gastritis in fibreoptic gastroscope biopsy specimens. *J Clin Path* 25:1-11.
15 Whitehead R, Roca M, Meikle DD, Skinner J, Truelove SC. The hist classification of duodenitis in fibrone biopsy specimens. *Digestion* 129-36.
16 Cheli R, Perasso A, Giacosa A. Dyspepsia and chrome gastritis. *Hepa enterology* 1983;30:21-3.
17 Venables CW. Duodenitis. *Scand J Gastroenterol* 1985;20 (suppl 109):
18 Bernersen B, Johnsen R, Straume B, Burhol PG, Jenssen TG, Stakkev Towards a "true" prevalence of peptic ulcer. *Gut* 1990;31:989-92.
19 Savary M, Miller G. *Der Oesophagus. Lehrbuch und endoskopische* Solothurn. Gassmann, 1977.
20 Johnsson F, Joelsson B, Gudmundsson K, Greiff L. Symptoms and end findings in the diagnosis of gastroesophageal reflux disease. *Gastroenterol* 1987;22:714-8.
21 Myren J, Sereck-Hanssen A. The gastroscopic diagnosis of gastritis. *Gastroenterol* 1974;9:457-62.
22 Owen DA. The diagnosis and significance of gastritis. *Pathology* 1979;1:247-71.
23 Snedecor GW, Cochran WG. *Statistical methods*. 6th ed. Iowa: Iow University Press, 1967:432-8.
24 Nie HH, Hull CH, Jenkins JG, Steinbrenner K, Bent DH. *Statistical for the social sciences*. 2nd ed. New York: McGraw Hill, 1975.
25 Spiro HM. Visceral viewpoints. Moynihan's disease? The diagn duodenal ulcer. *N Engl J Med* 1974;291:567-9.
26 Jorde R, Bostad L, Burhol PG. Asymptomatic gastric ulcer: a follow-u in patients with previous gastric ulcer disease. *Lancet* 1986;i:119-21.
27 Greenlaw R, Sheahann DG, DeLuca V, Miller D, Myerson D, Myer Gastroduodenitis: a broader concept of peptic ulcer disease. *Dig* 1988;25:660-72.
28 Strous W. A clinical, endoscopic and histopathologic study. *Q* 1985;56:593-600.
29 Danielsson A, Ek B, Nyhlin H, Steen L. The relationship between peptic ulcer, endoscopic duodenitis and symptomatic state after tre with cimetidine. *Ann Clin Res* 1980;12:4-12
30 Barlam RJ, Amerogo J, Kakavoulis T, Pollack DJ. Histological appear oesophagus, antrum and duodenum and their correlation with symp patients with a duodenal ulcer. *Gut* 1985;26:95-100.
31 Joffe SN, Rao SS. Symptoms of gastritis. *Scand J Gastroenterol* 1982;17 79):62-5
32 Cheli R, Giacosa A. Duodenal ulcer and chrome gastritis. *En* 1986;18:125-6.
33 Villako K, Tamm A, Savissar E, Ruttay M. Prevalence of antral and gastritis of an Estonian rural population. *Scand J Gastroenterol* 1976 22
34 Mackinnon M, Willing RL, Whitehead R. Cimetidine in the manage symptomatic patients with duodenitis. *Dig Dis Sci* 1982;27:217-9.
35 Toukan AU, Kamal MF, Amr SS, Arnaout MA, Abu-Romiych AS. duodenal inflammation in patients with non-ulcer dyspepsia. *Dig* 1985;30:313-20.

(*Accepted 7 January 1991*)

PAPER IV

Erosive Prepyloric Changes in Dyspeptics and Non-Dyspeptics in a Defined Population

The Sørreisa Gastrointestinal Disorder Study

B. BERNERSEN, R. JOHNSEN, B. STRAUME & P. G. BURHOL
Institute of Community Medicine, University of Tromsø, and Laboratory of Gastroenterology, Dept. of Medicine, University Hospital, Tromsø, Norway

Bernersen B, Johnsen R, Straume B, Burhol PG. Erosive prepyloric changes in dyspeptics and non-dyspeptics in a defined population. The Sørreisa gastrointestinal disorder study. Scand J Gastroenterol 1992, 27, 233–237

In this population-based endoscopic survey we found erosive prepyloric changes (EPC) in 38.5% of dyspeptics and 35.1% of non-dyspeptics. EPC were observed more frequently in men than in women in both groups. Occurrence of *Helicobacter pylori* was not associated with EPC. No common gastrointestinal symptoms were found to be associated with EPC. Endoscopic duodenitis of the duodenal bulb was found more frequently in subjects with EPC of the two highest grades than in subjects without EPC. Only the highest grade of EPC was associated with chronic gastritis. EPC were associated with cigarette smoking and, among women, also use of alcohol. We conclude that EPC constitute an endoscopic finding without relation to specific symptoms. These changes therefore do not represent a clinical entity, and it is doubtful whether this finding will give the clinician a better understanding of dyspepsia.

Key words: Erosive prepyloric changes; gastric mucosal erosions; gastritis; *Helicobacter pylori*; non-ulcer dyspepsia

Bjørn Bernersen, M.D., Institute of Community Medicine, Breivika, N-9000 Tromsø, Norway

Nesland & Berstad in 1985 (1) described an endoscopic diagnosis based on the presence of standing mucosal folds in the prepyloric region of the stomach (grade 1), sometimes with visible red spots and streaks (grade 2), and in the fully developed picture, called erosive prepyloric changes (EPC), erosions were also present (grade 3). The view that EPC constitute an independent clinical entity was supported in later studies, and EPC were suggested to have an acid-related pathogenesis (2). One author suggested EPC to be related to weakening of the mucosal defence with a defective mucus and bicarbonate barrier (3), whereas others have found EPC associated neither with *Helicobacter pylori* colonization nor with acute inflammation of the stomach mucosa (4).

EPC of grades 2 and 3 were found in 32% of patients with non-ulcer dyspepsia and in 18% of asymptomatic controls (1). This diagnostic entity was believed not to be connected with peptic ulcer disease (1). In another publication, however, the same authors showed reduced epigastric pain and degree of EPC on cimetidine therapy (5), whereas low-dose antacids and pirenzepine did not influence symptoms or the endoscopic picture (6).

The aim of this paper was to describe the occurrence of EPC in dyspeptics and non-dyspeptics in a general population. We also report on the relation between EPC and endoscopic and histologic findings and the associations between EPC and symptoms and possible predisposing factors, including *H. pylori*.

MATERIALS AND METHODS

From March to May 1987 all 2027 men and women, aged 20 to 69 years, of the municipality of Sørreisa in Northern Norway received a postal questionnaire with 119 questions on abdominal complaints, health, lifestyle, diet, and social conditions.

Subjects with confirmatory answers to the first two or the last of the following questions were classified as dyspeptics: 'Have you ever had abdominal pain of at least 2 weeks' duration?', and 'If yes, was the pain located to the upper abdomen?', and 'Have you ever had heartburn or acid regurgitation almost daily during at least 1 week?'

Of the 2027 persons invited, 88.9% returned the questionnaire. Dyspeptics without a history of peptic ulcer, gallstone, kidney stone, cardiac diseases, or abdominal surgery were offered an endoscopy. Corresponding non-dyspeptic controls matched for sex and age, within the same 10-year age groups, were randomly selected and offered an endoscopy as well. Non-dyspeptics refusing endoscopy were replaced in a second, similar procedure. Of 782 subjects invited to endoscopy, 619 men and women (79.2%) were endoscoped, of which 309 were dyspeptics and 310 non-dyspeptics. All were endoscoped within 1 month after returning their questionnaires. A detailed description of the methods is published elsewhere (7).

The study was approved by the regional committee of medical research ethics.

Table I. The age- and sex-specific percentages of erosive prepyloric changes (grades 1–3) in 309 dyspeptic and 310 non-dyspeptics, Sørr 1987

Age group, years	Dyspeptics						Non-dyspeptics					
	Men		Women		Total		Men		Women		Total	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
20–29	35	42.9	30	33.3	65	38.5	36	33.3	23	4.3	59	22.0
30–39	44	50.0	42	35.7	86	43.0	46	47.8	42	31.0	88	39.8
40–49	54	40.7	34	38.2	88	39.8	53	49.1	37	24.3	90	38.9
50–59	24	41.7	22	22.7	46	32.6	23	47.8	22	27.3	45	37.8
60–69	12	41.7	12	16.7	24	29.2	12	33.3	16	31.3	28	32.1
Total	169	43.8	140	32.1	309	38.5	170	44.1	140	24.3	310	35.1

Endoscopy

All endoscopies were performed by one of the authors (B. Bernersen), who is a trained endoscopist. The endoscopist was 'blinded' in the sense of not knowing whether he examined a dyspeptic or a non-dyspeptic. Subjects were offered intravenous premedication with 5 mg of a commercially available diazepam preparation (Diazemuls®, KabiVitrum AB, Stockholm, Sweden). Atropine was not given as premedication. Biopsy specimens for histologic examination were taken from the proximal and distal parts of the duodenum, from both the greater and the lesser curvatures of the antrum and corpus of the stomach and also from the lesions. Biopsy specimens for culture of *H. pylori* were taken from the lesser and from the greater curvature of the antrum approximately 3 cm proximal to the pyloric ring. Erosive prepyloric changes were noted and classified after air inflation of the stomach and before conducting the endoscope into the duodenum in accordance with the description by Nesland & Berstad (1).

Helicobacter pylori

Biopsy specimens for culture were placed in 0.5 ml of a glucose/saline solution (25% glucose in 0.9% saline solution), ground, and placed on one blood agar plate and one plate of brain–heart infusion agar with horseblood within 5 min after endoscopy. The plates were incubated in a Gas Pack jar at 37°C under microaerobic conditions (Gas generating box Campylobacter bioMerrieux). After 3–10 days the positive cultures of grey, translucent colonies were tested for urease, catalase, and oxidase activity. They were also Gram-stained for microscopic examination. The diagnosis of *H. pylori* was made when the enzyme reactions mentioned above were positive together with a typical Gram stain.

Histologic examination

The specimens were formalin-fixed and prepared in accordance with standard methods. Haematoxylin/eosin- and periodic acid-Schiff/Alcian blue-stained sections were interpreted at the Dept. of Histopathology at the University Hospital of Tromsø by one experienced pathologist, without any clinical or microbiologic information available. Inflammation in the gastric and duodenal mucosae was classi in accordance with Whitehead et al. (8) and, when ac inflammation was present, in accordance with Owen (9

Regression analysis

The following independent variables were explored finally assessed in a logistic regression: age; sex; daily smol (yes/no); number of cigarettes smoked daily; coffee sumption (none or less than 1 cup a day, 1–5 cups, and 6 or more a day); beer, wine, and liquor consumption (gra 0–2); nourishment as baby (mother's milk or not); regula of meals; excessive use of spices, ketchups, or mustard; us aspirin; use of non-steroidal antiinflammatory drugs; slee pills and ataraxics; and shift work (all yes/no); social st (4 grades); and physical activity (graded 1–4: sedent mode-rate, active, and hard training). Only the following v ables contributed significantly to the final model: sex; d smoking; and beer, wine, and liquor consumption.

The following symptoms were also explored in a sepa analysis similar to the procedure mentioned above: vari combinations of irritable bowel symptoms (in which a c bination of abdominal pain in the lower part of or the wh abdomen, relief of pain with bowel movement, loose frequent stools or very hard stools, and presence of muc stools were used); frequent upper abdominal pain or he burn; abdominal pain for the last 2 weeks; abdominal p of long duration; frequent globus sensation; nausea; h matemesis; blood with stools; melaena (all yes/no); nervous symptoms (graded 1–3 in accordance with freque of combinations of frequent headache, unspecific verti palpitations, and insomnia). None of these variables shov significance at any step of the analysis.

Statistical methods

Chi-square statistics were used to compare EPC in grou Age trends were tested with the Mantel–Haenszel chi-squ test. Logistic regression and adjustment for age and distribution by analysis of covariance were made in SPSSX statistical program. We analysed our data both 273 complete pairs and in groups. As the analyses gave

Table II. Percentage distribution and mean age in graded erosive prepyloric changes (EPC) in 309 dyspeptics and 310 non-dyspeptics aged 20–69 years, Sørreisa, 1987

Grade of EPC	Dyspeptics, $n = 309$				Non-dyspeptics, $n = 310$			
	n	%	Mean age, years	CI	n	%	Mean age, years	CI
No EPC	190	61.5	40.5	(38.8–42.2)	201	64.8	40.4	(38.7–42.1)
Grade 1	70	22.7	37.5	(35.0–40.0)	69	22.3	40.5	(38.1–42.9)
Grade 2	28	9.0	40.3	(36.0–44.6)	27	8.7	42.1	(38.0–46.2)
Grade 3	21	6.8	43.9	(39.3–48.5)	13	4.2	49.5	(43.7–55.3)

CI denotes 95% confidence interval.

Table III. The age- and sex-adjusted percentages of endoscopic findings in accordance with grading of erosive prepyloric changes (EPC) in 619 subjects aged 20–69 years, Sørreisa, 1987

Endoscopic findings	No EPC, $n = 391$		EPC grade 1, $n = 139$		EPC grade 2, $n = 55$		EPC grade 3, $n = 34$	
	%	CI	%	CI	%	CI	%	CI
Oesophagitis	9.9	(7.3–13.5)	10.2	(5.6–16.3)	11.9	(4.7–23.4)	4.5	(0.7–19.7)
Bile reflux	15.5	(12.1–19.5)	13.3	(8.1–20.0)	18.1	(9.1–30.9)	24.0	(10.7–41.2)
Duodenitis of the duodenal bulb	11.5	(8.6–15.3)	9.4	(5.0–15.4)	35.0	(22.3–48.6)	39.9	(22.9–57.9)
Deformity of the duodenal bulb	4.5	(2.8–7.1)	3.2	(1.5–7.7)	3.7	(0.4–12.5)	14.1	(4.9–31.0)
Duodenal ulcer	1.3	(0.4–3.0)			0.9	(0.1–3.2)		
Gastric ulcer	1.5	(0.6–3.4)	0.0		0.0		0.0	

CI denotes confidence interval.

same results, we have chosen to present results only from the total material.

RESULTS

EPC were found in 119 (38.5%) of the dyspeptics and 109 (35.1%) of the non-dyspeptics, a non-significant difference ($p = 0.40$). Table I shows the age and sex distribution of all grades of EPC together. EPC were observed more frequently in men than in women, both among dyspeptics and non-dyspeptics ($p = 0.0004$). The male to female ratio was 1.36 in dyspeptics and 1.8 in non-dyspeptics. Table II shows the mean age of those without EPC and of the subjects with the various grades of EPC. Non-dyspeptic subjects with EPC grade 3 had a slightly but significantly higher mean age than those with EPC grade 1 and those without EPC. There was no age trend within any of the gradings of EPC.

Table III shows the relations between EPC and endoscopic findings. EPC of grades 2 and 3 were associated with duodenitis of the duodenal bulb ($p < 10^{-6}$), and EPC of grade 3 had deformity of the duodenal bulb more frequently than those without EPC ($p = 0.036$). There were no such differences for the other endoscopic features listed.

Table IV shows the relation of EPC to histologic diagnoses and positive culture of *H. pylori*. There was no association between histologic gastritis and EPC. An analysis with the subtypes of gastritis showed more chronic atrophic gastritis ($p = 0.012$) and slightly more subacute gastritis ($p = 0.032$) in subjects with EPC grade 3 than in those without EPC. The frequency of *H. pylori*-positive cultures in EPC was the same as in subjects without EPC ($p = 0.19$).

An analysis of common gastrointestinal symptoms showed no significant association of any symptom or symptom complex with EPC. The logistic regression analysis of possible risk factors for EPC (Table V) showed that men were more likely to have EPC than women. This finding was consistent even after adjustment for smoking, consumption of alcoholic beverages, and occurrence of endoscopic duodenitis in an analysis of covariance. Smoking was positively associated with EPC. Moreover, EPC of grades 2 and 3 were positively associated with use of alcoholic beverages. In a sex-specific analysis the association of EPC with the degree of alcohol consumption was inconsistent with a significant association only in women. EPC were not associated with the reported use of aspirin or non-steroidal antiinflammatory drugs.

DISCUSSION

This study demonstrated that endoscopic findings described as erosive prepyloric changes are frequent in a general

Table IV. The age- and sex-adjusted percentages (and 95% confidence intervals) of histologic findings and positive culture of *Helicob pylori* in accordance with erosive prepyloric changes (EPC) in 619 subjects aged 20–69 years, Sørreisa, 1987

Histologic findings/ *Helicobacter pylori*	No EPC, $n = 391$		EPC grade 1, $n = 139$		EPC grade 2, $n = 55$		EPC grade 3, $n = 34$	
	%	CI	%	CI	%	CI	%	CI
Subacute gastritis	18.5	(12.0–19.5)	19.3	(13.1–26.8)	17.8	(8.8–30.5)	35.8	(19.8–53.5)
Chronic atrophic gastritis	52.6	(47.9–57.9)	47.1	(38.7–55.7)	40.0	(27.0–54.1)	76.6	(58.9–89.3)
Positive culture of *H. pylori*	42.7	(36.6–46.7)	39.2	(31.2–47.9)	33.2	(20.7–46.7)	56.4	(37.9–72.8)

CI denotes confidence interval.

Table V. Regression coefficients (beta) and odds ratio (OR) with corresponding 95% confidence intervals (CI) in a logistic regres analysis of erosive prepyloric changes (EPC), total and graded with significant independent variables in 619 men and women aged 2 years, Sørreisa, 1987

Independent variables	EPC total, $n = 228$			EPC grades 2 and 3, $n = 89$		
	Beta	OR	CI	Beta	OR	CI
Age	0.0005	1.00	(0.99–1.02)	0.0239	1.02	(1.00–1.04)
Sex (0–1)*	0.6859	1.99	(1.40–2.82)	0.4326	1.54	(0.94–2.54)
Use of alcohol (0–2)	0.0179	1.01	(0.79–1.31)	0.4211	1.52	(1.11–2.09)
Smoking (0–1)	0.5018	1.65	(1.18–2.32)	0.6478	1.91	(1.20–3.05)

* Female sex, value = 0; male sex, value = 1.

population. In our study dyspeptic subjects did not have EPC more frequently than non-dyspeptics. Moreover, the analyses did not reveal any specific symptoms that could increase the likelihood of making these endoscopic findings. On this point our study did not support the conclusion based on findings in a patient population and in asymptomatic volunteers, which suggested that the recognition of EPC may lead to a more accurate definition of a group with ulcer-like symptoms (1). It is more likely that studies using patients will be biased.

There is, however, a striking difference between sexes in that men are more likely to have EPC. This is a new finding, as patient populations showed a male to female ratio in EPC of 1.1 (1) and in gastric erosions of 0.98 (10). This difference was consistent after adjustment for sex differences in smoking, use of alcoholic beverages, and frequency of endoscopic duodenitis.

The analysis of possible risk factors in this study made it likely that various substances that usually may be regarded as noxious to the gastric mucosa might have some impact. Strangely, we found no association between EPC and the use of aspirin or non-steroidal antiinflammatory drugs, but this may be due to a lack of coincidence in point of time for intake of the drugs and the time of endoscopy. Our question to the participants was, however: 'Do you often take one or more of the following drugs listed: Aspirin etc?' Our study may show a possible noxious effect of cigarette smoking and alcohol. It is also possible that these substances, as mentioned, may act as stimulants of gastric secretion. Nesland & Berstad (1) found the same maxi acid output (MAO) in patients with EPC as in cont and lower MAO than in duodenal ulcer patients. Stu of EPC in patients showed, however, a significant impr ment measured by the grading scale of EPC in pati with EPC grades 2 and 3 treated for 4 weeks with cim dine (5), which may lead us to suspect an associatio EPC with acid secretion. In our study we have no dat this aspect, as acid secretion was not studied. Our st showed, however, a relation between EPC and endosc duodenitis of the duodenal bulb, which may sugge high gastric acid secretion (11).

The histologic picture in EPC is that of chronic gastr We studied multiple biopsy specimens taken in a standa ized pattern in our material, but not specimens especi designed to reveal erosions. We may therefore have mis some features of acute inflammation described in connec with erosions, as found by others (12).

H. pylori was not related to EPC to any extent exceed that of chronic gastritis, in agreement with an earlier p lication (4). For EPC grade 3 the number may be too sm to show an association with *H. pylori* despite the sho association with subacute and chronic gastritis.

EPC are an endoscopic finding without relation to spec symptoms in our study. They therefore do not represe clinical entity and are most unlikely to lead us to a be understanding of dyspepsia. The endoscopic feature may acid-related, although the information is controversial may be precipitated through cigarette smoking and possi

by use of alcoholic beverages. There are some problems to be solved for the understanding of this particular endoscopic feature, but it is questionable whether the term EPC is helpful for the clinician.

REFERENCES

1. Nesland AA, Berstad A. Erosive prepyloric changes in persons with and without dyspepsia. Scand J Gastroenterol 1985, 20, 222–228
2. Karvonen AL, Kekki M, Lehtola J, Sipponen P, Ihamäki T. Prepyloric erosions: an entity of its own among erosive gastric lesions. A morphologic and dynamic study of gastric mucosa in patients with gastric erosions. Scand J Gastroenterol 1987, 22, 1095–1101
3. Guslandi M, Ballarin E, Tittobello A. Deranged gastric mucus secretion in erosive prepyloric changes. Scand J Gastroenterol 1989, 24, 904–906
4. Berstad A, Alexander B, Weberg R, Serck-Hansen A, Holland S, Hirschowitz BI. Antacids reduce campylobacter pylori colonization without healing the gastritis in patients with nonulcer dyspepsia and erosive prepyloric changes. Gastroenterology 1988, 95, 619–624
5. Nesland AA, Berstad A. Effect of cimetidine in patients with non-ulcer dyspepsia and erosive prepyloric changes. Scand J Gastroenterol 1985, 20, 629–635
6. Weberg R, Berstad A. Low-dose antacids and pirenzipine in the treatment of patients with non-ulcer dyspepsia and erosive prepyloric changes. A randomized, double-blind, placebo-controlled trial. Scand J Gastroenterol 1988, 23, 237–243
7. Bernersen B, Johnsen R, Straume B, Burhol PG, Jenssen TG Stakkevold PA. Towards a true prevalence of peptic ulcer: the Sørreisa gastrointestinal disorder study. Gut 1990, 31, 989–992
8. Whitehead R, Truelove SC, Gear MWL. The histological diagnosis of chronic gastritis in fibreoptic gastroscope biopsy specimens. J Clin Pathol 1972, 25, 1–11
9. Owen DA. The diagnosis and significance of gastritis. Pathol Annu 1979, 1, 247–271
10. Karvonen AL, Lehtola J. Outcome of gastric mucosal erosions. A follow-up study of elective gastroscopic patients. Scand J Gastroenterol 1984, 19, 228–234
11. Kreunig J, Wal AM vd, Kuiper G, Lindeman J. Chronic non-specific duodenitis. A multiple biopsy study of the duodenal bulb in health and disease. Scand J Gastroenterol 1989, 24 Suppl 167, 16–20
12. Nesland AA, Berstad A, Serck-Hansen A. Histological findings in erosive prepyloric changes. Scand J Gastroenterol 1986, 21, 239–245

Received 27 August 1991
Accepted 22 October 1991

PAPER V

Is *Helicobacter pylori* the cause of dyspepsia?

Bjørn Bernersen, Roar Johnsen, Leif Bostad, Bjørn Straume, Ann-Inger Sommer, Per G Burhol

Abstract

Objective—To determine the association between infection with *Helicobacter pylori* and dyspepsia.

Design—Cross sectional study of dyspeptic subjects and age and sex matched controls identified by a questionnaire survey of all inhabitants aged 20-69. (Endoscopy, histological examination, and microbiological examinations of biopsies from the gastric mucosa were performed blind.)

Setting—Population based survey in Sørreisa, Norway.

Subjects—All 782 dyspeptic subjects (excluding those with a previous history of peptic ulcer, gall stones or kidney stones, and coronary heart disease) and controls were offered an endoscopy, of whom 309 dyspeptic subjects and 310 controls attended.

Main outcome measures—Prevalences of endoscopic and histological diagnoses and of cultures positive for *H pylori*.

Results—A high prevalence of positive cultures, increasing with age, was found in both dyspeptic subjects (48%) and non-dyspeptic controls (36%) ($p=0.004$). Positive cultures in both dyspeptic subjects and controls were strongly associated with histological gastritis (70%, 95% confidence interval 65·5 to 85·3; 60%, 52·7 to 67.7, respectively) and peptic ulcer (92%, 61·5 to 99·8; 64·1, 9·4 to 99·2, respectively). Only 3% of subjects with a histologically non-inflamed gastric mucosa had this infection (dyspeptic subjects 2%, 0·2 to 7·0; controls 4%; 1·2 to 8·8).

Conclusions—The relation between dyspeptic symptoms and *H pylori* is dubious; *H pylori* seems to have a pathogenetic role in gastritis and may be a contributing factor but not a cause of peptic ulcer.

Institute of Community Medicine, University of Tromsø N-9001, Tromsø, Norway
Bjørn Bernersen, *research fellow in gastroenterology*
Roar Johnsen, *research fellow in general practice*
Bjørn Straume, *assistant professor in epidemiology*

N-9012 University Hospital, N-9012 Tromsø, Norway
Leif Bostad, *consultant pathologist*
Ann-Inger Sommer, *senior researcher in microbiology*
Per G Burhol, *professor of gastroenterology*

Correspondence and requests for reprints to: Dr B Bernersen, Institute of Clinical Medicine, University of Tromsø, N-9000 Tromsø, Norway.

BMJ 1992;304:1276-9

Introduction

Dyspepsia requires costly management despite lack of knowledge of its causes. The rediscovery by Warren and Marshall[1] of curved bacilli in the gastric mucosa which were related to gastritis[1-3] has recharged the discussion about the cause of dyspepsia. A strong association between *Helicobacter pylori* and gastritis and peptic ulcer disease has been shown in patient populations.[1-4,8] *H pylori* has been declared an aetiologic agent of gastritis and even the cause of dyspepsia, though this is disputed.[9-12] Studies on asymptomatic volunteers have shown high prevalences of *H pylori* infection,[4,13,14] of up to 47% in the age group 60 to 69,[14] but there is little evidence of its prevalence in healthy, normal populations and of the concurrence of *H pylori* infection and symptoms of dyspepsia. Only one study on the occurrence of *H pylori* in a general popula has been published.[15] Population based data mandatory in considering *H pylori* as a pathogen agent in gastritis and peptic ulcer disease and possible cause of dyspepsia.[6,16]

As part of a population based study we examined endoscopy unselected subjects with dyspepsia matched non-dyspeptic controls to determine prevalence of *H pylori* infection and its relation endoscopic and histological diagnoses.

Subjects and methods

From March to May 1987 all inhabitants of municipality of Sørreisa in northern Norway aged 2 69 years, 2027 men and women, received a po questionnaire with 119 questions about abdom complaints, health, lifestyle, diet, and social conditi

All of the subjects answering positively to the two questions: "Have you ever had abdominal pai at least two weeks' duration?" and "If yes, was the located to the upper abdomen?" or the last questi "Have you ever had heartburn or acid regurgita almost daily during at least one week?" were sidered to have dyspepsia.

After exclusion of 89 dyspeptic subjects wit prior history of peptic ulcer, 15 with gall stone kidney stones, and 33 with coronary heart dis the remainder were offered an endoscopy free of cha Corresponding healthy, non-dyspeptic con matched for sex and age within the same 10 age group were randomly selected and offered endoscopy. The controls reported that they had n experienced dyspeptic symptoms and also had n consulted their general practitioner with dyspepsia 2027 subjects invited, 1802 (88·9%) returned questionnaire. Of 782 subjects invited to endosc 619 (79·2%) (309 dyspeptic subjects and 310 dyspeptic controls) had endoscopy, all within month after returning their questionnaires. A deta description of the methods has been published where.[17] The study was approved by the regi committee for medical research ethics.

ENDOSCOPY

All endoscopies were performed by BB, who trained endoscopist. He was "blinded" in the sens not knowing whether he was examining a dyspepti a non-dyspeptic subject. Endoscopic findings classified according to criteria described by Savary Miller (oesophagitis),[18] Johnsson *et al* (hiatus herni Myren and Serck-Hanssen (endoscopic gastritis gastroduodenal reflux),[20] Nesland and Berstad (ero

aged 20-69, Sørreisa, Norway, 1987

Age group	Dyspeptic subjects (n=309)						Controls (n=310)					
	Men		Women		Total		Men		Women		Total	
	No	No (%) positive	No	No (%) positive	No	No (%) positive	No	No (%) positive	No	No (%) positive	No	No (%) positive
20-29	35	11 (31)	30	9 (30)	65	20 (31)	36	8 (22)	23	3 (13)	59	11 (
30-39	44	24 (54)	42	24 (57)	86	48 (56)	46	17 (37)	42	16 (38)	88	33 (
40-49	54	24 (44)	34	20 (59)	88	44	53	12 (23)	37	21 (57)	90	33 (
50-59	24	9 (38)	22	9 (41)	46	18 (39)	23	12 (52)	22	11	45	23 (
60-69	12	9 (75)	12	8 (67)	24	17 (71)	12	4 (33)	16	8	28	12 (
Total	169	77 (46)	140	70 (50)	309	147 (48)	170	53 (31)	140	59 (42)	310	112 (

prepyloric changes),[21] Venables (duodenitis),[22] and Bernersen *et al* (peptic ulcer and deformed duodenal bulb).[17]

Biopsy specimens for histological examination were taken from the proximal and distal parts of the duodenum, from both the greater and lesser curvatures of the corpus and antrum of the stomach, and from all lesions as well. Biopsy specimens for culture were also taken from the lesser and from the greater curvature of the antrum about 3 cm proximal to the pyloric ring. The endoscopes (Olympus gastroscope type GIF-Q 20) and biopsy forceps were cleaned and thereafter disinfected in a commercially available glutaraldehyde solution (Korsolin; Norforma, Rud, Norway) between each endoscopy.

MICROBIOLOGICAL EXAMINATION

Biopsy specimens for culture were placed in 0·5 ml of glucose/saline solution (25% glucose in 0·9% saline solution), ground, and cultured on blood agar and on brain-heart infusion agar containing horse (5% v/v) blood within five minutes after endoscopy. The media were incubated in a Gas Pack jar at 37°C under microaerobic conditions (Gas generating box Campylobacter bioMerrieux). After three to 10 days any positive cultures, appearing as grey translucent colonies were tested for urease, catalase, and oxidase activities. They were also Gram stained for microscopic examination. The number of positive colonies was evaluated using a semiquantitative scale. *H pylori* was identified on the basis of positive urease, catalase and oxidase reactions together with a typical microscopic appearance on Gram staining. There were no problems with contamination. The microbiologist had no clinical information on the subjects available.

TABLE II—*Prevalence adjusted for age and sex (95% confidence interval) of cultures positive for H pylori from antral gastric mucosa, according to endoscopic diagnosis*

Endoscopic diagnosis	Dyspeptic subjects (n=309)		Controls (n=310)	
	No	No (%) positive	No	No (%) positive
Normal	79	42 (53) (41·6 to 64·5)	116	41 (35) (25·8 to 43·4)
Oesophagitis	36	16 (44) (27·9 to 61·9)	25	6 (24) (9·4 to 45·1)
Gastritis	74	42 (57) (44·7 to 68·2)	63	21 (33) (22·0 to 46·3)
Biliary reflux	54	31 (57) (43·2 to 70·8)	43	15 (35) (21·0 to 50·9)
Peptic ulcer	12	11 (92) (61·5 to 99·8)	3	2 (64) (9·4 to 99·2)
Erosive prepyloric changes	119	49 (41) (32·0 to 50·2)	109	41 (38) (28·3 to 47·0)
Deformed duodenal bulb	19	13 (69) (43·5 to 87·4)	10	4 (39) (12·2 to 73·8)
Duodenitis of duodenal bulb	61	31 (51) (37·7 to 63·9)	30	8 (27) (12·3 to 45·9)

TABLE III—*Prevalence adjusted for age and sex (95% confidence interval) of cultures positive for H pylori from antral gastric mucosa, according to histological diagnosis*

Histological diagnosis	Dyspeptic subjects (n=309)		Controls (n=310)	
	No	No (%) positive	No	No (%) positive
Normal gastric mucosa	101	2 (2) (0·2 to 7·0)	132	5 (4) (1·2 to 8·8)
Gastritis	208	145 (70) (65·5 to 85·3)	178	107 (60) (52·7 to 67·7)
Chronic superficial gastritis	134	102 (76) (68·7 to 83·0)	117	81 (69) (61·1 to 71·6)
Chronic atrophic gastritis	190	146 (70) (60·8 to 74·8)	152	95 (62) (54·4 to 70·3)
Chronic active gastritis	78	47 (61) (48·5 to 71·2)	55	35 (63) (49·3 to 75·9)
Duodenitis in proximal duodenum	180	86 (48) (40·4 to 55·4)	196	78 (40) (32·4 to 46·5)

HISTOLOGICAL EXAMINATION

The biopsy specimens, labelled with refere numbers, were formalin fixed and prepared accor to standard methods. Thin sections stained v haematoxylin and eosin and periodic acid Schiff Alcian blue were examined in the department of hi pathology at the University Hospital by one exp enced pathologist (LB) without any available clin or microbiological information. Inflammation of gastric and duodenal mucosa was classified accor to Whitehead *et al*[23 24] or, when active inflammation present, according to Owen.[25]

STATISTICAL METHODS

We analysed our data for both 273 comp matched pairs of subjects and all 619 cases controls, with similar results. We present the res from the unpaired cases and controls. χ^2 and Cochr Mantel-Haenszel statistics were used to compare prevalence of *H pylori* infection overall and in strati groups. Trends in age were tested by the Man Haenszel χ^2 test. Adjustments for different age and distributions in the diagnostic subgroups were m by analysis of covariance with the SPSS-X statist program. Odds ratios and confidence intervals w calculated according to Fleiss.[26] Confidence inter of proportions were calculated from the unadjus numbers.

Results

H pylori was cultured from 259 (41·8%) of participating subjects (table I). Significantly m positive cultures were obtained from dyspep subjects than from non-dyspeptic controls (48% 36%, p=0·004). The odds ratios were 1·85 (9 confidence interval 1·16 to 2·95) for men and 1·37 (0 to 2·26) for women and were only marginally differ (p=0·053). There was a linear increasing trend prevalence of *H pylori* with age in both dyspep subjects (p=0·036) and controls (p=0·003), wh persisted when sex was controlled for.

The prevalence of *H pylori* in the endosco diagnostic subgroups, both with and without pep ulcer, was compared with that in the group w normal endoscopic findings, controlling for age, s and dyspeptic symptoms (table II). Only in the pep ulcer group was it higher than in the group wit normal endoscopic diagnosis (p=0·035).

Positive culture of *H pylori* was strongly related histological findings in the gastric mucosa (table II The prevalence of *H pylori* was rare (3%) in th subjects with a histologically normal gastric muco When histological gastritis was divided into subtyp according to the degree of inflammation, there w only insignificant differences among positive cultu for the respective subtypes. When histological gastri of the antrum and corpus were studied separate however, the prevalence of *H pylori* infection w significantly higher when the chronic active gastri

the corpus (70% *v* 43%, p=0·002).

Discussion

The strength of this study is its population base and its design to avoid observer bias. Clinical information was not available to the endoscopist, pathologist, or microbiologist. Dyspepsia has no generally accepted definition,[27,28] and endoscopic and histological findings may vary with different intensity and duration of the dyspeptic symptoms.[29] We chose to restrict the definition to the most commonly accepted symptoms. We found a high prevalence of *H pylori* in both the dyspeptic subjects and non-dyspeptic controls but a strong association between *H pylori* and peptic ulcer and histological gastritis. Subjects with a histologically normal mucosa had an almost negligible prevalence of *H pylori*. The rate of positive cultures of 3% in this group is within the margin of error for histological findings. It seems reasonable to believe that a histologically normal gastric mucosa is incompatible with *H pylori* infection.

Other authors have used detection of the organism in stained tissue preparations,[1,16] in culture, or both,[4,7,8,13,30,31] and, occasionally, detection of serum antibodies to the organism as criteria for the presence of *H pylori* infection.[32] Discrepancies exist between findings based on various diagnostic procedures.[14,33] We used only isolation of *H pylori* as a criterion, and thus we may have detected somewhat lower prevalences than if we had added together all criteria for the presence of *H pylori* in the gastric mucosa. On the other hand, a rather low occurrence of 3% in subjects with a histologically normal mucosa indicates a high specificity. This finding agrees with results in a Finnish population based on similar criteria of normality, in which *H pylori* was present in 5% of the subjects with a normal antral mucosa.[30]

The prevalences in non-dyspeptic controls in our study were within the same range as in previous studies,[4,13,14] showing that *H pylori* infection is quite common even among subjects without dyspepsia, whereas the prevalence of *H pylori* infection in dyspeptic subjects was lower than previously reported from patient populations.[7,9] This may partly reflect our exclusion of subjects with a previously diagnosed peptic ulcer.

Even though there was a higher prevalence of *H pylori* infection in dyspeptic than non-dyspeptic subjects, 43% of positive cultures were found among non-dyspeptic controls. Some authors have suggested that this organism plays a major part in non-ulcer dyspepsia.[6,34] The high prevalence in non-dyspeptic controls indicates that *H pylori* infection alone is unlikely to provoke dyspeptic symptoms.

Our study confirms the association between gastritis and *H pylori* infection. The interesting point is why *H pylori* is absent in a third of subjects with histological gastritis. One may suggest other properties of the mucosa in these subjects, but a clinical course in which the inflammatory process proceeds after the disappearance of *H pylori* may also be proposed.[35]

Peptic ulcer was the only endoscopic finding associated with a significantly higher frequency of *H pylori* infection than endoscopically normal mucosa. Peptic ulcer is associated with gastritis. Antral gastritis is found in a high proportion of patients with duodenal ulcer,[36] and gastric ulcers are usually found in an area with chronic gastritis.[36,37] As *H pylori* infection in our study was strongly associated with gastritis our finding of a prevalence of *H pylori* infection in peptic ulcer as high as 86·5% may support the theory of a pathogenetic role for this organism in peptic ulcer disease. *H pylori* infection and gastritis were, however, found in a

heavily weighs against *H pylori* infection being
sufficient cause of peptic ulcer. The role of *H pylori* ir
causal context may parallel that of gastric acid ar
pepsin. A strong association was found betwe
H pylori infection and duodenal ulcer.[4,5] If deformity
the duodenal bulb is the result of a previous duoden
ulcer a stronger association than we found wou
be expected between this deformity and *H pyl*
infection. However, this may also reflect the possibili
that the *H pylori* infection resolves with the active ulc
and is not a chronic infection.

Our cross sectional design offers limited possibilit
for causal interference, and the causal role of *H pyl*
should be explored in a longitudinal design in whi
the active *H pylori* infection, serological finding
gastric mucosal histological findings, and sympto
are surveyed in a cohort.

In conclusion, *H pylori* infection of the stomach w
common both in dyspeptic subjects and in no
dyspeptic controls with an increasing prevalence wi
age. This infection is strongly associated with hist
logical gastritis and peptic ulcer, which may suppo
the theory of a causal role for *H pylori* in gastritis and
least a role as a pathogenetic factor in peptic ulc
disease. *H pylori*, like gastric acid and pepsin, may b
necessary but not a sufficient cause of peptic ulcer. T
association with symptoms of dyspepsia, on the oth
hand, is dubious.

1 Warren JR, Marshall B. Unidentified curved bacilli on gastric epithelium
active chronic gastritis. *Lancet* 1983;i:1273-5.
2 Doenges JL. Spirochetes in the gastric glands of Macacus rhesus and hum
without definite history of related disease. *Proc Soc Exp Med*
1938;38:536-8.
3 Freedberg AS, Barron LE. The presence of spirochetes in human gas
mucosa. *American Journal of Digestive Diseases* 1940;7:443-5.
4 Langenberg ML, Tytgat GN, Schipper MEI, Rietra PJGM, Zanen
Campylobacter-like organisms in the stomach of patients and hea
individuals. *Lancet* 1984;a:1348-9.
5 Goodwin CS, Armstrong JA, Marshall BJ. Campylobacter pyloridis, gastr
and peptic ulceration. *J Clin Pathol* 1986;39:353-65.
6 Dooley CP, Cohen H. The clinical significance of Campylobacter py
Ann Intern Med 1988;108:70-9.
7 Petrross CW, Appleman MD, Cohen H, Valenzuela JE, Chandrasom
Lane LA. Prevalence of Campylobacter pylori and association with a
mucosal histology in subjects with and without upper gastrointes
symptoms. *Dig Dis Sci* 1988;33:649-53.
8 Rauws EAJ, Langenberg W, Houthoff HJ, Zanen HC, Tytgat GNJ. Camp
bacter pylorudis-associated chronic active antral gastritis. *Gastroenter*
1988;94:33-40.
9 Marshall BJ, Armstrong JA, McGechie DB, Glancy RJ. Attempt to
Koch's postulates for pyloric campylobacter. *Med J Aust* 1985;142:436-
10 Morris A, Nicholson G. Ingestion of Campylobacter pyloridis causes gas
and raises fasting gastric pH. *Am J Gastroenterol* 1987;82:192-9.
11 Peterson WL, Lee EL, Feldman M. Gastric campylobacter-like organism
healthy humans: correlation with endoscopic appearance and mu
histology. *Gastroenterology* 1986;90:1585 (abstract).
12 Bartlett JG. Campylobacter pylori: fact or fancy? *Gastroenterology* 198
229-38.
13 Barthel JS, Westblom TU, Havey AD, Gonzales F, Everett ED. Gastritis
Campylobacter pylori in healthy, asymptomatic volunteers. *Arch Intern*
1988;148:1149-51
14 Dooley CP, Cohen H, Fitzgibbons PL, Baner M, Appleman MD, Perez-
GI, *et al*. Prevalence of Helicobacter pylori infection and histologic gas
in asymptomatic persons. *N Engl J Med* 1989;321:1562-6.
15 Sipurala M, Sipponen P, Kekki M. Campylobacter pylori in a samp
Finnish population: relations to morphology and functions of the ga
mucosa. *Gut* 1988;29:909-15.
16 Talley NJ, Phillips SF. Non-ulcer dyspepsia: potential causes and p
physiology. *Ann Intern Med* 1988;108:865-79.
17 Bernersen B, Johnsen R, Straume B, Burhol PG, Jenssen TG, Stakkevole
Towards the "true" prevalence of peptic ulcer. *Gut* 1990;31:989-92.
18 Savary M, Miller G. *Der Oesophagus. Lehrbuch und endoskopischer A*
Solothurn: Gassmann, 1977.
19 Johnsson F, Joelsson B, Gudmunsson K, Greuff L. Symptoms and endos
findings in the diagnosis of gastroesophageal reflux disease. *Sca*
Gastroenterol 1987;22:714-8.
20 Myren J, Serck-Hanssen A. The gastroscopic diagnosis of gas
Scand J Gastroenterol 1974;9:457-62.
21 Nesland AA, Berstad A. Erosive prepylonic changes in persons with
without dyspepsia. *Scand J Gastroenterol* 1985;20:222-8.
22 Venables CW. Duodenitis. *Scand J Gastroenterol* 1985;20(suppl 109):91
23 Whitehead R, Truelove SC, Gear MWL. The histological diagnosis of ch
gastritis in fibreoptic gastroscope biopsy specimens. *J Clin Pathol* 197
1-11.
24 Whitehead R, Roca M, Meikle DD, Skinner J, Truelove SC. The histol
classification of duodenitis in fibreoptic biopsy specimens. *Digestion* 19
129-36.
25 Owen DA. The diagnosis and significance of gastritis. *Pathology A*
1979;1:247-1.
26 Fleiss JL. *Statistical methods for rates and proportions*. New York: Wiley, 1
27 Heatley RV, Rathbone BJ. Dyspepsia: a dilemma for doctors? *I*
1987;n:779-82.

1988;i:576-9.
29 Johnsen R, Bernersen B, Straume B, Forde OH, Bostad L, Burhol PG. Prevalences of endoscopic and histological findings in subjects with and without dyspepsia. *BMJ* 1991;302:749-52.
30 Coghlan JG, Gilligan D, Humphries H, McKenna D, Dooley C, Sweeney E, *et al.* Campylobacter pylori and recurrence of duodenal ulcers—a 12 month follow-up study. *Lancet* 1987;ii:1109-11.
31 Loffeld RJLF, Potters HVJP, Stobbenringh E, Flending JA, Van Spreeuwel JP, Arends JW. Campylobacter associated gastritis in patients with non-ulcer dyspepsia: a double blind placebo controlled trial with colloidal bismuth subcitrate. *Gut* 1989;30:1206-12.
32 Al-Moagel MA, Evans DH, Abdulghani ME, Adam E, Evans DJ, Malaty HM, *et al.* Prevalence of Helicobacter pylori infection in Saudi Arabia, and comparison of those with and without upper gastrointestinal symptoms. *Am J Gastroenterol* 1990;85:944-7.
33 Marshall BJ, Warren JR, Francis GJ, Langton SR, Goodwin CS, Blincow ED, *et al.* Rapid urease test in the management of Campylobacter pyloridis-associated gastritis. *Am J Gastroenterol* 1987;82:200-10.
34 Marshall BJ, McGechie DB, Rogers PA, Glancy RJ. Pyloric campylobacter infection and gastroduodenal disease. *Med J Aust* 1985;142:439-44.
35 Villako K, Maards H, Tammur R, Keevallik R, Peetsalu M, Sipponen P, *et al.* Helicobacter pylori infestation and the development and progression of chronic gastritis: results of long-term follow-up examinations of a large sample. *Endoscopy* 1990;22:114-7.
36 Tatsuta M, Iishi H, Okuda S. Location of peptic ulcers in relation to atrophic fundal gastritis by chromoendoscopic follow up examinations. *Dig Dis Sci* 1986;31:7-11.
37 Lawson HH. Effect of duodenal contents on the gastric mucosa: experimental conditions. *Lancet* 1964;i:469-72.

(Accepted 24 February 1992)

10. APPENDIX

Sørreisa-undersøkelsen

Fordøyelsesbesvær eller magesårlignende plager er svært vanlig. Bare et fåtall av de som har magesårlignende plager har imidlertid magesår. Vi vet ikke hvor mange som har slike plager i en vanlig befolkning. Heller ikke vet vi årsaken til slike plager, eller om personer med slike plager vil utvikle magesår senere.

Det vil derfor være av stor betydning for forståelsen og dermed behandlingen av slike plager å kunne gjennomføre en undersøkelse over fordøyelsesbesvær eller magesårlignende plager i Sørreisa. Denne undersøkelsen er et samarbeidsprosjekt mellom Kommunehelsetjenesten i Sørreisa, Gastroenterologisk seksjon, Medisinsk avdeling, Regionsykehuset i Tromsø og institutt for samfunnsmedisin, Universitetet i Tromsø.

Som det vil fremgå av vedlagte spørreskjema, ønsker vi å kartlegge følgende som kan være av betydning:

- Generelle forhold.
- Mageplager og beslektede forhold.
- Andre plager.
- Slektsforhold med tanke på mulig arvelighet.
- Spisevaner som kan virke utløsende og forverrende.
- Likeså forbruk av kaffe, te, tobakk, alkohol og medikamenter.
- Yrkesmessige og sosiale forhold.

De fleste som har eller har hatt fordøyelsesbesvær vil senere få tilbud om en nærmere undersøkelse av magen på kommunelegekontoret i Sørreisa ved overlege Bjørn Bernersen. Det er viktig at så mange som mulig møter opp til denne undersøkelsen.

Vi håper at alle som får tilsendt dette spørreskjemaet tar bryet med å fylle det ut og å returnere det så fort som mulig. All deltagelse er frivillig.

Innsendte spørreskjemaer vil bli gjennomgått av medisinsk personell og behandlet strengt konfidensielt på samme måte som legejournaler. Alle opplysninger blir lagret på EDB og gjort utilgjengelig for uvedkommende.

Vennlig hilsen

Per A. Stakkevold
kommunelege I

Bjørn Bernersen
overlege

Idar Elvemo
kommunelege II

GENERELT

1. Dato for utfylling av ditt skjema: ..... dag mnd. år 001

2. Etternavn: _____ 002.1

   Fornavn: _____ .2

3. Fødselsdato: ..... dag mnd. år 003

4. Kjønn: (sett kryss i den ruten som passer) ..... Kvinne: ☐ 004.1

   Mann: ☐ .2

5. Adresse: _____ 005

   Postnr.:_____ Poststed: _____

6. Sivilstand:

   Sett kryss i den ruten som passer best.

   — Ugift: ..... ☐ 006.1
   — Samboende: ..... ☐ .2
   — Gift: ..... ☐ .3
   — Separert: ..... ☐ .4
   — Skilt: ..... ☐ .5
   — Enke/enkemann: ..... ☐ .6

Mageplager

7. Har du noen gang hatt smerter eller «verk» i magen som har vart i minst to uker? (Omgangssyke («reksiuke») regnes ikke med) (Sett kryss i den ruten som passer)

   JA ☐ 007 1
   NEI ☐ .2

   Hvis «NEI», gå direkte til spørsmål nr. 29.
   Hvis «JA», fortsett med spørsmål nr. 8.

8. Sitter smertene eller «verken» i

   Sett kryss i den ruten som passer best.

   — øvre del av magen? ..... ☐ 008 1
   — nedre del av magen? ..... ☐ 2
   — hele magen? ..... ☐ 3

9. Angi så nøyaktig som mulig hvilket årstall du første gang merket smertene eller «verken» i magen: ..... Årstall _____ 009

10. Har smertene eller «verken» i magen noen gang vært tilstede hver dag i mer enn to måneder? (Sett kryss i den ruten som passer)

    JA ☐ 010 1
    NEI ☐ 2

11. Har du hatt smerter eller «verk» i magen de siste to ukene? ..... (Sett kryss i den ruten som passer)

    JA ☐ 011 1
    NEI ☐ 2

12. Er smertene eller «verken» jevnt over tilstede

    Sett kryss i den ruten som passer best.

    — i perioder av ukers varighet? ☐ 012
    — i perioder av måneders varighet? ☐
    — bestandig? ..... ☐

13. Hvilke måneder er smertene eller «verken» i magen vanligvis verst?

    Sett kryss i den eller de rutene som passer.

    — Januar—februar: ..... ☐ 013
    — Mars—april: ..... ☐
    — Mai—juni: ..... ☐
    — Juli—august: ..... ☐
    — September—oktober: ..... ☐
    — November—desember: ..... ☐
    — Ingen forandring gjennom året: ☐

14. Blir smertene eller «verken» i magen vanligvis

    Sett kryss i den ruten som passer best.

    — bedre når du spiser? ..... ☐ 014
    — verre når du spiser? ..... ☐
    — upåvirket når du spiser? ..... ☐

15. Blir smertene eller «verken» i magen vanligvis

    Sett kryss i den ruten som passer best.

    — bedre ved fysiske anstrengelser? ..... ☐ 015.1
    — verre ved fysiske anstrengelser? ☐ .2
    — upåvirket ved fysiske anstrengelser? ..... ☐

16. Hender det at du våkner om natten av smertene eller «verken» i magen? ..... JA ☐ NEI ☐ 016.1 .2
(Sett kryss i den ruten som passer)

17. Har du søkt lege på grunn av smertene eller «verken» i magen? ..... JA ☐ NEI ☐ 017.1 .2
(Sett kryss i den ruten som passer)

18. Hvis «JA», hvor mange ganger har du søkt lege siste året på grunn av smertene eller «verken» i magen? ..... Antall _____ 018

19. Har du vært henvist til, eller innlagt i sykehus på grunn av smertene eller «verken» i magen? JA ☐ NEI ☐ 019.1 .2
(Sett kryss i den ruten som passer)

20. Hvis «JA», angi hvilket sykehus.
(Skriv navnet her): _____ 020.1
Hvilket år ble du henvist eller undersøkt siste gang? ..... Årstall _____ .2

21. Har du vært sykemeldt for smertene eller «verken» i magen? JA ☐ NEI ☐ 021.1 .2
(Sett kryss i den ruten som passer)

22. Hvis «JA», angi hvor mange uker du har vært sykemeldt for smertene eller «verken» i magen i løpet av de siste 12 månedene: .... Antall uker _____ 022

23. Har du brukt syrenøytraliserende midler som Balancid, Link, Novaluzid, Alminox, Antacid, Titralac, Natron eller Wismutmixtur mot smertene eller «verken» i magen? ..... JA ☐ NEI ☐ 023.1 .2
(Sett kryss i den ruten som passer)

24. Hvis «JA», har disse midlene hjulpet mot smertene eller «verken» i magen? ..... JA ☐ NEI ☐ 024.1 .2
(Sett kryss i den ruten som passer)

25. Har du fått andre medikamenter på resept for smertene eller «verken» i magen? ..... JA ☐ NEI ☐ 025.1 .2
(Sett kryss i den ruten som passer)

Hvis «JA», kryss av for den gruppen under spørsmålene 26, 27 og 28, hvor du eventuelt finner navnet på det medikamentet du har fått. Om nødvendig se etter på resept, medisinglass eller pakning om du finner navnet. Svar også på om dette medikamentet har hjulpet eller ikke hjulpet mot smertene eller «verken» i magen.

26. Cimal, Cimetid, Gastrobitan, Tagamet, Ranacid eller Zantac? ..... JA ☐ NEI ☐ 026.1 .2
(Sett kryss i den ruten som passer)
Hvis «JA», har dette hjulpet mot smertene eller «verken» i magen? ..... JA ☐ NEI ☐ .3 .4
(Sett kryss i den ruten som passer)

27. Egazil Duretter, Daricon, Gastrozepin, Librax, Oximin, Ulcoban? ..... JA ☐ NEI ☐ 027.1 .2
(Sett kryss i den ruten som passer)
Hvis «JA», har dette hjulpet mot smertene eller «verken» i magen? ..... JA ☐ NEI ☐ .3 .4
(Sett kryss i den ruten som passer)

28. Surmontil? ..... JA ☐ NEI ☐ 028.1 .2
(Sett kryss i den ruten som passer)
Hvis «JA», har dette hjulpet mot smertene eller «verken» i magen? ..... JA ☐ NEI ☐ .3 .4
(Sett kryss i den ruten som passer)

29. Har du hatt sure oppstøt, halsbrann eller brystbrann nesten daglig i minst en uke? .. JA ☐ NEI ☐ 029.1 .2
(Sett kryss i den ruten som passer)

30. Er du ofte plaget av kvalme eller oppkast?.. JA ☐ NEI ☐ 03
(Sett kryss i den ruten som passer)

31. Har du noen gang kastet opp blod? ..... JA ☐ NEI ☐ 03
(Sett kryss i den ruten som passer)

32. Har du vansker med å svelge, eller følelse av at maten stopper opp i halsen eller brystet? JA ☐ NEI ☐ 0
(Sett kryss i den ruten som passer)

33. Er du ofte plaget av oppblåsthet, rumling i magen eller rikelig luftavgang fra endetarmen? JA ☐ NEI ☐ 0
(Sett kryss i den ruten som passer)

34. Hvis «JA», blir oppblåstheten eller rumlingen bedre etter avføring eller luftavgang fra endetarmen? ..... JA ☐ NEI ☐ 0
(Sett kryss i den ruten som passer)

35. Er avføringen din vanligvis
Sett kryss i den ruten som passer best.
— normal? ..... ☐ 0
— løs? ..... ☐
— hard og perlet? ..... ☐
— vekslende løs og hard? ..... ☐

36. Har du i perioder tre eller flere avføringer daglig? ..... JA ☐ NEI ☐ 0
(Sett kryss i den ruten som passer)

37. Har du i perioder avføring sjeldnere enn hver tredje dag? ..... JA ☐ NEI ☐ 0
(Sett kryss i den ruten som passer)

38. Har du ofte sett slim i avføringen? ..... JA ☐ NEI ☐ 0
(Sett kryss i den ruten som passer)

39. Har du noen gang sett friskt, rødt blod i avføringen? ..... JA ☐ NEI ☐ 0
(Sett kryss i den ruten som passer)

40. Har du noen gang hatt beksvart eller tjærelignende avføring? ..... JA ☐ NEI ☐ 0
(Sett kryss i den ruten som passer)

41. Hvis «JA», brukte du forut for dette jerntabletter eller jernmikstur? ..... JA ☐ NEI ☐ 0
(Sett kryss i den ruten som passer)

42. Har du noen gang hatt hemorroider eller sår/rifter i endetarmsåpningen? ..... JA ☐ NEI ☐ 0
(Sett kryss i den ruten som passer)

43. Har du eller har du fått påvist magesår? ..... JA ☐ NEI ☐ 0
(Sett kryss i den ruten som passer)

44. Er du operert for magesår? ..... JA ☐ NEI ☐ 0
(Sett kryss i den ruten som passer)

45. Har du eller har du hatt gallestein? ..... JA ☐ NEI ☐ 0
(Sett kryss i den ruten som passer)

46. Har du vært operert for noe annet i magen? .. JA ☐ NEI ☐ 0
(Sett kryss i den ruten som passer)

47. Hvis du har vært operert i magen, angi da så nøyaktig som mulig når du ble operert i magen siste gang ..... Årstall _____ 0

— og angi også ved hvilket sykehus
(Skriv navnet på sykehuset her): _____

Andre plager

48. Har du eller har du hatt angina pectoris (hjertekrampe)? ..... JA ☐ NEI ☐ 048.1 .2
(Sett kryss i den ruten som passer)

49. Har du eller har du hatt hjerteinfarkt (sår på hjertet)? ..... JA ☐ NEI ☐ 049.1 .2
(Sett kryss i den ruten som passer)

50. Har du eller har du hatt annen hjertesykdom? JA ☐ NEI ☐ 050.1 .2
(Sett kryss i den ruten som passer)

51. Har du sukkersyke? ..... JA ☐ NEI ☐ 051.1 .2
(Sett kryss i den ruten som passer)
Hvis «JA», bruker du

Sett kryss i den ruten som passer best.
- — insulin? ..... ☐ .3
- — tabletter for sukkersyke? ..... ☐ .4
- — bare diett? ..... ☐ .5

52. Har du eller har du hatt nyrestein? ..... JA ☐ NEI ☐ 052.1 .2
(Sett kryss i den ruten som passer)

53. Har du hatt allergiske reaksjoner i øyne/nese (høysnue e.l.)? ..... JA ☐ NEI ☐ 053.1 .2
(Sett kryss i den ruten som passer)

54. Har du hatt allergiske reaksjoner i luftveier (astma)? ..... JA ☐ NEI ☐ 054.1 .2
(Sett kryss i den ruten som passer)

55. Har du hatt allergiske reaksjoner i hud (utslett)? ..... JA ☐ NEI ☐ 055.1 .2
(Sett kryss i den ruten som passer)

56. Har du hatt allergiske reaksjoner i mage-tarm? ..... JA ☐ NEI ☐ 056.1 .2
(Sett kryss i den ruten som passer)

57. Har du noen gang reagert allergisk på medisiner? ..... JA ☐ NEI ☐ 057.1 .2
(Sett kryss i den ruten som passer)

58. Har du ofte en eller flere av følgende plager?

Sett kryss i den eller de rutene som passer.
- — Hodepine: ..... ☐ 058.1
- — Svimmelhet: ..... ☐ .2
- — Hjertebank: ..... ☐ .3
- — Søvnvansker: ..... ☐ 4
- — Menstruasjonsplager: ..... ☐ .5

59. Har du leddgikt eller ofte ledd- og muskelsmerter? ..... JA ☐ NEI ☐ 059.1 .2
(Sett kryss i den ruten som passer)

60. Plages du med forkjølelsessår eller munnsår?

Sett kryss i den ruten som passer best.
- — Aldri: ..... ☐ 060.1
- — Sjelden: ..... ☐ .2
- — Av og til: ..... ☐ .3
- — Ofte: ..... ☐ 4

61. Hvordan synes du din helsetilstand er nå?

Sett kryss i den ruten som passer best.
- — Meget bra: ..... ☐ 061.1
- — Bra: ..... ☐ 2
- — Midt i laget: ..... ☐ .3
- — Dårlig: ..... ☐ .4
- — Meget dårlig: ..... ☐ .5

62. Oppgi din egen høyde og vekt nå:
- — Høyde (i cm): ..... _____ cm 062.1
- — Vekt (i kg): ..... _____ kg .2

63. Angi, såfremt du kan, om du som spebarn fikk:

Sett kryss i den ruten som passer best.
- — Brystmelk: ..... ☐ 063.1
- — Kunstig ernæring (flaske): .... ☐ 2
- — Begge deler: ..... ☐ 3
- — Vet ikke: ..... ☐ 4

Slekt

Antall

64. Angi hvor mange nålevende søsken du har: .. _____

Antall

65. Angi hvor mange av dine søsken som er døde: ..... _____

Antall

66. Angi hvor mange barn du har: ..... _____

67. Har noen av disse i din familie hatt magesår?

Sett kryss i den eller de rutene som passer.
- — Ektefelle/samboer: ..... ☐
- — Mor: ..... ☐
- — Far: ..... ☐
- — Søster: ..... ☐
- — Bror: ..... ☐
- — Barn: ..... ☐
- — Ingen: ..... ☐

68. Har noen av disse i din familie hatt fordøyelsesplager uten å ha hatt magesår?

Sett kryss i den eller de rutene som passer.
- — Ektefelle/samboer: ..... ☐
- — Mor: ..... ☐
- — Far: ..... ☐
- — Søster: ..... ☐
- — Bror: ..... ☐
- — Barn: ..... ☐
- — Ingen: ..... ☐

Spisevaner

69. Spiser du til faste tider?

Sett kryss i den ruten som passer best.
- — Alltid: ..... ☐
- — Vanligvis: ..... ☐
- — Av og til: ..... ☐
- — Så godt som aldri: ..... ☐

70. Spiser du vanligvis frokost hver dag? ..... JA ☐ NEI ☐
(Sett kryss i den ruten som passer)

71. Spiser du vanligvis middag hver dag? ..... JA ☐ NEI ☐
(Sett kryss i den ruten som passer)

72. Spiser du vanligvis etter kl. 10 om kvelden? JA ☐ NEI ☐
(Sett kryss i den ruten som passer)

73. Spiser du vanligvis mellom hovedmåltidene? JA ☐ NEI ☐
(Sett kryss i den ruten som passer)

74. Har du for vane å salte maten ekstra? ..... JA ☐ NEI ☐
(Sett kryss i den ruten som passer)

75. Har du for vane å bruke mye krydder? . .... JA ☐ NEI ☐
(Sett kryss i den ruten som passer)

76. Har du for vane å bruke mye sennep? ..... JA ☐ NEI ☐
(Sett kryss i den ruten som passer)

77. Har du for vane å bruke mye ketchup? ..... JA ☐ NEI ☐
(Sett kryss i den ruten som passer)

Kosthold

78. Hva slags brød spiser du vanligvis?

Sett kryss i den ruten som passer best.
- — Loff: ..... ☐
- — Fint (lyst) brød: ..... ☐
- — Grovt (mørkt) brød: ..... ☐
- — Klibrød: ..... ☐

79. Hvor mange brødskiver spiser du vanligvis daglig?

Sett kryss i den ruten som passer best.

– Mindre enn 2 skiver:	☐	079.1
– 2–4 skiver:	☐	.2
– 5–6 skiver:	☐	.3
– 7–12 skiver:	☐	.4
– 13 eller flere skiver:	☐	.5

80. Bruker du vanligvis fibertilskudd som kli, klibrød, klikavring, kliknekkebrød, Musli, frokostblanding o.l.? (Sett kryss i den ruten som passer)

JA	☐	080.1
NEI	☐	.2

81. Hvor mange glass melk drikker du vanligvis daglig?

Sett kryss i den ruten som passer best.

– Drikker ikke melk:	☐	081.1
– Mindre enn 1 glass:	☐	.2
– 1–2 glass:	☐	.3
– 3–4 glass:	☐	.4
– 5 glass eller flere:	☐	.5

82. Hvor ofte spiser du vanligvis grønnsaker til middag eller som egen rett? (Her menes både rå og kokte grønnsaker.)

Sett kryss i den ruten som passer best.

– Sjelden eller aldri:	☐	082.1
– Omtrent en gang i uken:	☐	.2
– 2–3 ganger i uken:	☐	.3
– 4–5 ganger i uken:	☐	.4
– Omtrent daglig:	☐	.5

Fysisk aktivitet

83. Hvor ofte mosjonerer du eller deltar du i fysisk trening av minst 20 minutters varighet og slik at du blir svett eller andpusten?

Sett kryss i den ruten som passer best.

– Sjelden eller aldri:	☐	083.1
– Ukentlig:	☐	.2
– Flere ganger i uken:	☐	.3
– Daglig:	☐	.4

84. Hvor lang tid bruker du til mosjon eller trening av den typen som er nevnt ovenfor?

Sett kryss i den ruten som passer best.

– Mindre enn 30 min i uken:	☐	084.1
– Mellom 30 min og 1 time i uken:	☐	.2
– Mellom 1 og 2 timer i uken:	☐	.3
– Mer enn 2 timer i uken:	☐	.4

Kaffe/te

85. Hvor mange kopper kaffe drikker du vanligvis daglig?

Sett kryss i den ruten som passer best.

– Drikker ikke kaffe, eller mindre enn en kopp:	☐	085.1
– 1–4 kopper:	☐	.2
– 5–8 kopper:	☐	.3
– Mer enn 9 kopper:	☐	.4

86. Hvis du drikker kaffe; har du minsket kaffeforbruket i løpet av de siste 5 år? (Sett kryss i den ruten som passer)

JA	☐	086.1
NEI	☐	.2

87. Hvor mange kopper te drikker du vanligvis daglig?

Sett kryss i den ruten som passer best.

– Drikker ikke te, eller mindre enn en kopp:	☐	087.1
– 1–4 kopper:	☐	.2
– 5–8 kopper:	☐	.3
– Mer enn 9 kopper:	☐	.4

Tobakk

88. Røker du sigaretter daglig (enten ferdige eller rullede)? (Sett kryss i den ruten som passer)

JA	☐	088
NEI	☐	

89. Hvis «JA», røker du mindre nå enn for 5 år siden? (Sett kryss i den ruten som passer)

JA	☐	089
NEI	☐	

90. Hvis «NEI», har du røkt sigaretter tidligere? (Sett kryss i den ruten som passer)

JA	☐	090
NEI	☐	

91. Hvis du har røkt sigaretter tidligere; hvor lenge er det siden du sluttet?

Sett kryss i den ruten som passer best.

– Mindre enn 3 mnd.:	☐	091.
– Mellom 3 mnd. og 1 år:	☐	
– Mellom 1 og 5 år:	☐	
– Mer enn 5 år:	☐	

92. For alle som røker eller som har røkt sigaretter tidligere, angi hvor mange år du tilsammen har røkt sigaretter daglig?

Antall år

____ 092

93. Angi hvor mange sigaretter du røker/eller du røkte tidligere daglig?

Antall

____ 093

94. Røker du daglig annen tobakk som sigarer, sigarillos eller pipetobakk? (Sett kryss i den ruten som passer)

JA	☐	094.
NEI	☐	

95. Bruker du vanligvis snus eller skråtobakk daglig? (Sett kryss i den ruten som passer)

JA	☐	095.
NEI	☐	

96. Hvis «JA», angi hvor mange esker snus eller skråtobakk du bruker ukentlig:

Antall

____ 096

Alkohol

97. Smaker du fra til til annen alkoholholdige drikker som øl, vin eller brennevin? (Sett kryss i den ruten som passer)

JA	☐	097.1
NEI	☐	.2

Hvis «JA»:

98. Hvor ofte pleier du å drikke øl?

Sett kryss i den ruten som passer best.

– Aldri, eller noen få ganger i året:	☐	098.1
– 1–2 ganger i måneden:	☐	.2
– Omtrent 1 gang i uken:	☐	.3
– 2–3 ganger i uken:	☐	.4
– Omtrent hver dag:	☐	.5

99. Hvor ofte pleier du å drikke vin?

Sett kryss i den ruten som passer best.

– Aldri, eller noen få ganger i året:	☐	099.1
– 1–2 ganger i måneden:	☐	.2
– Omtrent 1 gang i uken:	☐	.3
– 2–3 ganger i uken:	☐	.4
– Omtrent hver dag:	☐	.5

100. Hvor ofte pleier du å drikke brennevin?

Sett kryss i den ruten som passer best.

– Aldri, eller noen få ganger i året:	☐	100.1
– 1–2 ganger i måneden:	☐	.2
– Omtrent 1 gang i uken:	☐	.3
– 2–3 ganger i uken:	☐	.4
– Omtrent hver dag:	☐	.5

Medikamenter

101. Bruker du ofte ett eller flere av følgende medikamenter?
— Albyl, Albyl-E, Alka-Seltzer, Antineuralgica, Dispril, Globentyl, Globoid, Paraflex eller Paraflex comp.: ..... JA ☐ NEI ☐ 101.1 .2
(Sett kryss i den ruten som passer)

102. Bruker du ofte ett eller flere av følgende medikamenter?
— Brufen, Clinoril, Confortid, Donobid, Felden, Indocid, Napren, Napren-E eller Naprosyn: ..... JA ☐ NEI ☐ 102.1 .2
(Sett kryss i den ruten som passer)

103. Bruker du ofte sovemedisiner?..... JA ☐ NEI ☐ 103.1 .2
(Sett kryss i den ruten som passer)

104. Bruker du ofte nervemedisiner?..... JA ☐ NEI ☐ 104.1 .2
(Sett kryss i den ruten som passer)

Yrke

105. Nåværende hovedyrke:

Sett kryss i den ruten som passer.

— Hjemmeværende husmor:	☐ 105.1
— Skoleelev/student:	☐ .2
— Industri/verksted/anleggs/bygnings/ sprengnings/gruvearbeide:	☐ .3
— Jordbruks/skogbruksarbeide:	☐ .4
— Fisker/sjømann:	☐ .5
— Kontor/handels/hotell/servicearbeide:	☐ .6
— Helse/lærer/annet undervisningsarbeide:	☐ .7
— Landtransport (sjåfør m.v.):	☐ .8
— Arbeidsledig:	☐ .9
— Under attføring:	☐ .10
— Uføretrygdet/alderstrygdet/pensjonert:	☐ .11
— Annet:	☐ .12

— Angi evt. yrkesbetegnelse her:

_____

106. Har du skiftarbeide? ..... JA ☐ NEI ☐ 106.1 .2
(Sett kryss i den ruten som passer)

107. Angi antall år du har vært på din siste arbeidsplass: ..... Antall år _____ 107

108. Må du i forbindelse med arbeide/skolegang overnatte utenfor hjemmet? ..... JA ☐ NEI ☐ 108.1 .2
(Sett kryss i den ruten som passer)

109. Hvis «JA», hvordan overnatter du?

Sett kryss i den ruten som passer best.

— I ordinær bopel/leilighet:	☐ 109.1
— På hybel:	☐ .2
— På hotell/pensjonat:	☐ .3
— I anleggsbrakke:	☐ .4
— På annen måte:	☐ .5

Sett kryss i den ruten som passer best.
— Meget godt: .....
— Godt: .....
— Dårlig: .....
— Trives ikke: .....

111. Angi hvor mange års skolegang du har medregnet folkeskole og framhaldsskole eller 9-årig grunnskole? ..... Antall _____

Sosiale forhold

112. Angi antall familiemedlemmer (deg selv medregnet) som bor i din husstand: ..... Anta _____

113. Er noen i din husstand 10 år eller yngre?.... JA ☐ NEI ☐
(Sett kryss i den ruten som passer)

114. Trenger noen i din husstand utenom barna spesielt tilsyn eller pleie? ..... JA ☐ NEI ☐
(Sett kryss i den ruten som passer)

115. Hvordan var de økonomiske forhold i familien under oppveksten din?

Sett kryss i den ruten som passer best.
— Meget gode: .....
— Gode: .....
— Vanskelige: .....
— Meget vanskelige: .....

116. Hvordan vil du beskrive din økonomiske situasjon nå?

Sett kryss i den ruten som passer best.
— Meget god: .....
— God: .....
— Vanskelig: .....
— Meget vanskelig: .....

117. Har du de siste to månedene følt deg ute av stand til å mestre dine vanskeligheter?

Sett kryss i den ruten som passer best.
— Aldri eller sjelden: .....
— Av og til: .....
— Ofte: .....
— Nesten hele tiden: .....

118. Har du de siste to månedene følt deg «nedfor»?

Sett kryss i den ruten som passer best.
— Aldri eller sjelden: .....
— Av og til: .....
— Ofte: .....
— Nesten hele tiden: .....

119. Føler du at du har dårlig tid, også når det gjelder daglige gjøremål?

Sett kryss i den ruten som passer best.
— Aldri eller sjelden: .....
— Av og til: .....
— Ofte: .....
— Nesten hele tiden .....

Denne undersøkelsen er støttet av firmaene
SEARLE NORGE A/S og SMITH KLINE & FRENCH