One of the most important bits of evidence for selection in man are the characteristics for which human populations are polymorphic. One of the most notable cases of polymorphism in man that is currently generating a lot of interest is the secretor state. This genetic marker with polymorphic nature has proved to be highly useful in the study of population genetics. The present study deals with two important facets of this genetic marker. One, which relates to basic polymorphic nature of the trait i.e., the differences in the frequencies of the secretor types at the population level. Their maintenance in sizable proportions, in itself is suggestive of the fact that the secretor system is subject to natural selection. The second most important aspect dealt with is the potential of secretor system as a disease marker.

As a first step to this study, the distribution of ABO blood groups and secretor types was studied in the normal healthy population of north west India, represented by three endogamous groups of people, the Jat Sikhs, the Khatris and the Brahmins. No marked intergroup differences were observed in the frequency distribution of alleles at the loci for ABO blood groups and ABH secretion. The Jat Sikhs showed a somewhat higher incidence of secretors than the other two groups, but the differences were statistically non-significant. The quantitative assay of secreted antigens in saliva showed that the 'H' substance was secreted in greater
strength in blood group O individuals in all the three caste
groups. A and B substances were likewise secreted in greater
amount in blood groups A and B respectively than in blood
groups AB. But for a somewhat higher mean titre score of A
substance in Jat Sikhs and of B substance (in B secretors)
in Brahmins, no marked intergroup differences were observed
in the quantitative scores of secreted antigens. The in-
cidence of aberrant secretion was the highest in Khatri
(5.9%) followed by Jat Sikhs (4.6%) and Brahmins (3.4%) in
that order. It is evident from the values of sample statis-
tics (Mean S.D. and S.E.) that the observed differences in
the three caste groups are due to chance more often than
not. The distribution by and large portray a similar pattern of variation of their antigenic characters. Although,
the three caste groups, at present, represent three distinct
gene pools, they are essentially one group of people in the
sense that they share a common racial substratum with
predominantly Mediterranean ethnic affinities. Their close
genetic relatedness along with the fact that they have
shared a common ecological niche for many generations, may
account for basic similarities in the qualitative as well as
quantitative expression of ABH antigens in these popula-
tions.

The next important question relates to the operation of
selection. Researches into the association of diseases and
blood groups have provided us with growing body of reliable
statistical evidence that selection operates on ABO blood groups system. During the last few years immense interest has also been generated in the secretor system as a potential disease marker. The genetic marker relating to secretor system possess slightly but certainly different survival values and influence health and survival of the individuals. A most valuable approach to study the relationship between these genetic markers and diseases is by investigating their distribution in patients suffering from various diseases. In some conditions, infectious or otherwise, they would depart from their normal frequencies, indicating that persons with particular blood groups and secretor state are unduly susceptible to the disease in question. The role of secretor state in the aetiology of disease is discussed herein the context of some noninfectious and infectious diseases prevalent in this region (North-West India).

NONINFECTIONOUS DISEASES:

In this category, gastrointestinal tract disorders command immediate attention because in individuals who are secretors, substances with ABO(H) specificity are present in high concentration in upper part of gastrointestinal tract. The most provocative results are the associations reported between duodenal ulcers and blood group O nonsecretors. The association between blood group O and ulcers was not con-
firmed in the first report of a study by Clarke and his Coworkers (1955). Clarke then used paired sib method of controls and discovered a very significant association between ulceration and secretor phenotypes of the individuals. He observed that the duodenal ulceration is likely to develop approximately 45% more often in nonsecretor than in the secretors. His data on the sibship studies also suggested that the relationship between nonsecretion and duodenal ulcer may hold within families. A protective role was suggested for ABH substances. (Glynn et al. 1957, Szulman 1960, 1962).

As reported by previous workers, our data too showed a significantly increased prevalence of nonsecretors among patients of duodenal ulcers. The association was particularly strong with group O nonsecretor state which occurred with a five fold higher incidence in patients. The raised incidence of blood group O, mostly at the expense of blood group A suggested a negative association of A antigens with duodenal ulceration. Quantitative assessment of secreted antigens in saliva showed that H substance was present in relatively low concentration in patients of duodenal ulcers. Other gastrointestinal tract disorders like gastritis, oesophagitis also showed a higher incidence of nonsecretors which was clearly reflected in their respective relative incidence values. The differences when examined in terms of the chisquare ($X^2$) values were statisti-
cally nonsignificant indicating that the departure from the normal frequencies was of lesser order in these patients and required a more sensitive test that the chi-square to be discerned. Woolf's (1955) identification and estimation of associations between blood groups and diseases has an added advantage that the estimated parameter is directly meaningful and is not influenced by the variations in the incidence of either disease or the blood group and secretor phenotype, so that the estimates are readily compared by weighting. Significant departures were also seen in higher concentration of A and B substances in AB patients than in A and B group patients.

Several hypotheses have been put forward which might explain the relationship between duodenal ulceration and blood group O and ABH nonsecretion. Vesley and Kubickova (1969) showed that the gastric acidity was significantly more in blood group O as compared to the other blood groups. They agreed with the view that action of the gene of blood group O is due to their influence on the morphological and biochemical structure of the mucosa and other tissues of the gastrointestinal tract. The relationship between gastric acidity and blood group O indicates that higher acidity is one of the factors responsible for the development and severity of duodenal ulceration. A lack of any association of the secretor state and ABO blood groups with non ulcer dyspepsia seems to be in accord with this hypothesis. As
there is no excess of blood group O nonsecretors and hence no greater acidity that can cause ulceration in these patients of dyspepsia'. Aird (1954) thought that various blood group substances might confer different degrees of protection against ulcerative agents.

Bhalla (1990) generated new evidence based on the distribution of secretor types in man and non-human primates to establish a correlation between lectins in diet and ABH polymorphism. He developed the hypothesis of "selection-relaxation" to account for sustained high frequency of non-secretors in the advanced human societies in contrast to the low frequency of recessive gene (se) diminishing to zero in many primitive human societies and its complete absence in apes and monkeys. Emphasizing the protective role of secreted antigens against deleterious effect of lectins on gastric mucosa, Bhalla (1990) postulated that, "the ability to secretor ABH substances in saliva and other glandular secretions was, perhaps, of paramount adaptive significance at a stage, in the early history of man, when he was eating raw food (rich in lectins) like other animals. With the invention of fire making techniques, food habits of early man witnessed a radical change from raw to cooked food. This, in all likelihood, resulted in the reversal of negative selection pressure bearing upon the nonsecretor allele leading to its establishment and maintenance in human
populations at frequencies much above the level of its mutation rate."

The predisposition of O nonsecretors to ulceration along with the observation that mean titre scores of H substance in the ulcer patients are lower in comparison to those of controls, suggest of a possible protective action of 'H' substance against ulcerative agents. These data lend support to the conclusion that the genes at ABO as well as secretor loci influence predisposition to duodenal ulceration.

Analysis of blood group and secretor state data of 74 vitiligo patients failed to show any correlation with the ABO(H) system.

INFECTIONOUS DISEASES:

Many years of researches have established that certain bacteria, protozoa and helminths have antigens that are related to blood group substances. These facts suggest that particular organisms might be resisted unequally by subjects possessing different blood groups and secretor status, either because of naturally occurring antibodies or because of ability to produce antibodies to antigens resembling those possessed by the host as a result of immunological tolerance. Vogel and his coworkers (1960) expounded these propositions in terms of immunological mechanisms. They said
that individuals are immunologically handicapped in the production of antibody against viruses or bacteria which carry antigenic specificities similar to those of their own blood group substances (cf Otten '67). This was found to hold true in most of the bacterial infections. A strong association of nonsecretors particularly of A and B blood groups has been reported with certain streptococcal infections as in rheumatic fever and rheumatic heart disease and also in throat infections. The present study focussed attention on oral disorders due to streptococcal infections such as dental caries and periodontitis. The results showed a significantly greater propensity of nonsecretors to develop dental caries and periodontitis. Quantitative assessment showed lower mean titre scores of A and B substances in A and B secretors than in AB secretors of dental caries and periodontitis patients. Because blood grouping of all dental caries and periodontitis patients tested for secretor state could not be done, the limitations of studying the secretor state in individual blood group categories was posed. These limitations notwithstanding the weaker secretors of A and B substances in patients of dental caries to periodontitis and greater resistance of secretors to these streptococcal infections seem to suggest an inhibitory effect of ‘H’ substance on the growth of bacteria. Haverkorn (1969) had earlier showed a higher incidence of RF
(Rheumatic fever) and RHD (Rheumatic heart disease) in non-secretors of A and B blood groups. The observations that secretors of ABO(H) substances have a significantly reduced risk of streptococcal infections suggests that the presence of group specific substances in glandular secretions may render the streptococci in some way more susceptible to body's normal immunological defenses.

HELICOBACTER PYLORI

Ever since the discovery of Helicobacter pylori there is an uncritical acceptance of the importance of this organism in the pathogenesis of gastrointestinal diseases. More than 70-90% of duodenal ulcer patients have been found to be colonised by Helicobacter pylori (Marshall et al.'84 b and Grahn D.Y'89). Knowing the association of Peptic ulceration with blood groups and secretor state, an attempt was made in the present study to find out whether the frequency of ABO blood groups and secretor types would differ in patients harbouring Helicobacter pylori infection than those who tested negative for this infection. A higher frequency of nonsecretors was recorded in Helicobacter pylori positive cases. The data was further analysed to see the correlation between blood groups, secretor state and Helicobacter pylori colonisation in duodenal ulcer and non ulcer dyspepsia patients. 75.3% of duodenal ulcers were found
to be colonised by Helicobacter pylori against only 34.2% of nonulcer dyspepsia patients, lending support to the previous findings wherein Helicobacter pylori was found to be strongly implicated in the pathogenesis of duodenal ulcers. Further, the results showed a positive association of non-secretor state and blood group 0 with Helicobacter pylori colonisation in duodenal ulcer patients. The nonulcer dyspepsia cases did not show any association of secretor state with Helicobacter pylori infection. A low relative incidence of blood group A and a statistically significant negative association of blood group A with Helicobacter pylori infection was found in the pooled samples of patients of duodenal ulcers and nonulcers dyspepsia. Quantitative assay revealed higher strength of ABH substances in AB Helicobacter pylori patients. However, H substance was secreted in lower concentration in Helicobacter pylori positive duodenal ulcer patients than in Helicobacter pylori negative duodenal ulcer patients, while in nonulcer dyspepsia no such differences were noticed. Thus a close association of nonsecretors and weaker strength of H substance in duodenal ulcers was evident with Helicobacter pylori infection. The nonsecretor state together with Helicobacter pylori colonisation seemed to be a host-susceptible factor in duodenal ulceration.

In an earlier study, Nikanne et al. (1990) had reported that there was no correlation between ABO blood groups,
secretor state and Helicobacter pylori colonisation. The results of the present study are thus at variance from those of Nikanne et al. (1990). Discrepancies in the findings of the two studies may be ascribed to the following two reasons: Firstly, Nikanne and his coworkers assessed the Helicobacter pylori status by finding antibodies to Helicobacter pylori, while in the present study, diagnosis of Helicobacter pylori infection was made by rapid urease test, grams staining, culture of the organism and histopathology. Secondly, Nikanne et al. (1990) had not assessed the correlation of Helicobacter pylori, blood groups and secretor state with basic disease state.

CONCLUSION

In the quest to find out the biological significance of secretor state, the present study brought forth and highlighted some important associations with certain disease (Table 64). Quantitative assessment of the secreted ABH substances in saliva lent further support to our hypothesis of greater susceptibility of nonsecretor state to some diseases and also to a sequeale of bacterial infections. These observations when viewed in the light of previous studies were also helpful in suggesting plausible mechanisms to explain the physiological basis of relationship between blood group antigens and susceptibility to diseases.
The broad picture that has emerged from the analysis of the data pertaining to ABH secretion of secreted antigens and their concentration in body fluids in a variety of diseases shows that susceptibility to gastrointestinal tract disorders and infectious diseases 'in general' do seem to have some bearing on the secretor state and blood group make up of an individual. The ABO(H) group specific substance
have functional, physiological roles in the life processes of the organisms. Certain lines of experimental research designed to lead to an understanding of the detailed function of these blood groups must precede eventual knowledge of their relationship to natural selection. This is dictated by the fact that selection operates on the functional manifestations of a trait (Buettner Janusch '1959).