

of degenerate point inverses on I . By the above theorem, we may suppose that for each open subinterval I_0 of I , $I_0 \cdot K$ is either empty or of measure > 0 .

Define, for $x \in I$, $g(x) = x$ minus the sum of lengths of nondegenerate intervals of constancy of f on $(0, x)$. Then $g(x)$ is continuous and monotone, because for $x_1 < x_2$,

$$0 \leq g(x_2) - g(x_1) \leq x_2 - x_1.$$

Define, for $p \in J$, $h(p) = gf^{-1}(p)$. Then, since g is constant on each set $f^{-1}(p)$, h is single-valued. Also, it is continuous because if UCI is open, $g^{-1}(U)$ is open by continuity of g and is an inverse set for f since f and g generate the same decomposition of I . Thus $fg^{-1}(U)$ is open in J and this is $h^{-1}(U)$. Finally, h is 1-1, because if $p, q \in J$, $p \neq q$, and $x_1 \in f^{-1}(p)$, $x_2 \in f^{-1}(q)$, then for $x_1 < x_2$ we have $g(x_1) < g(x_2)$ since the measure of $K \cdot (x_1, x_2)$ is > 0 .

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¹ For a direct elementary proof of this well-known topological theorem see, for example, the author's book *Topological Analysis* (Princeton University Press, 1958), p. 26.

NOTE ON THE EPIDEMIOLOGY OF PEPTIC ULCER

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Cecil and Loeb's *Textbook of Medicine* states (9th ed., 1955, p. 863): (1) Peptic ulcer occurs in the lower esophagus, in the stomach, and in the upper part of the duodenum. (2) The lesion occurs at all ages, and typically in a definite constitutional type—lean rather than stocky. (3) About 10 per cent of all persons suffer at some time in their lives from a chronic gastric or duodenal ulcer. (4) Males are afflicted about four times more frequently than females. (5) At autopsy, gastric ulcer is more frequent than duodenal, but duodenal is more frequently encountered clinically. An older book, Osler and McCrae's *The Principles of Medicine*, states (9th ed., 1923, p. 481): The incidence appears to differ in different localities and to be higher in England and Europe than in this country.

These statements are for clinicians; they have a statistical-epidemiological sound and, as the total experience of clinicians in respect to peptic ulcer probably greatly exceeds that of epidemiologists, should be given a good deal of weight in thinking about the disease. That peptic ulcer, whether or no it was more prevalent in Britain than here, was more in the mind of British than of American public health officers appeared clear to me from the discussions I heard in Glasgow in 1945–1946 as compared with those I had heard here in 1923–1946.

For the statistics of epidemiology of peptic ulcer, as for those of other diseases, there may be a considerable difference between those based on incidence or duration or autopsies or registered deaths. Incidence figures are hard to obtain on a national or other regional basis so as to make possible comparison between different places or different times, and the same is true of figures for duration or autopsies. My comments here will be on reported deaths, and divided as are the international

causes into gastric ulcer (540, formerly 117a) and duodenal ulcer (541, formerly 117b).

Scotland 1943.—Discussions in Glasgow centered on the most recent report of the Registrar-General for Scotland (the eighty-ninth, for 1943). Male deaths attributed to gastric ulcer were 230; female, 88—a sex ratio of 2.6. For duodenal ulcer, the figures were $M = 267, F = 36; M/F = 7.6$. Thus statistically with respect to sex ratio of deaths, the two diseases (or sites of the same disease?) were behaving very differently. Taken together, $M/F = 4.0$, exactly the figure in Cecil and Loeb (for relative incidence?). But the difference between the ratios 2.6 and 7.4 is highly significant by the criterion usually applied.

Female deaths from duodenal ulcer are too few to make comparison with female deaths from gastric ulcer, but male deaths can be compared; the question is how best to do it. The total numbers of deaths from gastric and duodenal ulcer, 230 and 267 respectively, do not differ significantly if regarded as arising from very low rates; yet I believe they must be taken into consideration in discussing age distribution. There are few deaths from either under 30 or over 80 years of age and they will be two of the age groups; in between, the figures will be for 5-year intervals.

Age	0-29	30-4	35-9	40-4	45-9	50-4	55-9	60-4	65-9	70-4	75-9	80 up
Gastric	8	13	14	20	19	19	27	28	28	27	15	12
Duodenal	8	16	26	35	21	27	45	24	29	15	13	8
O - C	±0.6	±0.4	±4.5	±5.5	±0.5	±2.3	±6.3	±3.9	±1.6	±7.6	±2.0	±2.7

Gastric seems more regular than duodenal; O - C means the observed less the calculated values as they would be for a χ^2 computation. Although a χ^2 test should not be applied in this case and would turn out nonsignificant if applied, it seems probable that the values of O - C are a good way in which to get a picture of the relative age distribution.¹ They show that except for very minor variations duodenal deaths are relatively high to age about 60 and gastric thereafter. If a 2×2 table be set up for age above and below 60 and deaths from gastric versus duodenal ulcer, the χ^2 value comes out at over 10, which is beyond the usual table.

The differences in sex ratio and age distribution led me to wonder whether gastric and duodenal ulcer were not in fact somewhat different diseases.

United States 1950-1959.—In this period, in the United States the statistical situation was very different from that in Scotland a dozen years earlier and indeed was changing during the decade. The figures can be found in the *U.S. Mortality Statistics*, which is so widely available that I shall not quote the data but only give the results. At the beginning of the period, white male deaths from gastric ulcer (540) were running well above those from duodenal (541); at the end, they were well below. For white females, gastric ulcer deaths ran steadily above duodenal, remaining in about the same proportions (56% G, 44% D). The trend equations summarize the information as follows:

Males Gastric	3,353	+ 33.84 t	Duodenal	3,555	+ 113.4 t
Females Gastric	1,071	+ 69.46 t	Duodenal	839	+ 60.6 t
% Fem. Gastric	24.0	+ 0.994 t	Duodenal	18.9	+ 0.623 t

Here, t is in years from the middle of the decade, January 1, 1955.

The last line gives the per cent female (rather than the sex ratio); it has been steadily higher for gastric ulcer than for duodenal, and the lead has been increasing. The

sex ratios for the two kinds of peptic ulcer have not been anything like so different as in Scotland above, but they have been significantly different, though behaving much alike in that they have both been decreasing about 0.18 per annum.²

These comments may be made. (1) As I use deaths rather than death rates, comparisons between different places and times cannot be made without some consideration of populations and their age distributions; but the sex ratios of gastric and duodenal ulcer differ in Scotland in 1943 and the United States so much that resort to population differences is unnecessary. (2) The departures from the trend in the number of cases of death from gastric ulcer are not much greater than could be expected from the size of the samples, and the excess is due to a very large number of deaths in 1958; the deaths from duodenal ulcer depart from rectilinearity systematically, the first two and the last two being negative averaging 126 and the middle six being positive averaging 84. This is very different behavior from the gastric cases, and the populations are the same with the same age distribution for the two ten-year series. (3) For females, the numbers are smaller, the deviations from trend are systematic judged by their signs but are so small as not to be much larger than might be expected from chance. For "per cent female" much the same is true.

With respect to age distribution, we note that in 1950, deaths from gastric ulcer much exceeded those from duodenal ulcer, whereas in 1959 the opposite was the case; it is therefore necessary to discuss relative differences as for the case of Scotland. In both these years and in 1953 and 1956, a similar situation is found in that, relatively speaking, there is an excess of gastric ulcer in early life, up to about the age of 25, and in late life, after an age of about 60, whereas between these ages duodenal ulcer deaths exceed gastric for males; and the phenomenon is highly significant.³

Smoking and Ulcer.—Of the three large prospective studies of smoking and deaths, the two by Doll and Hill and by Dorn are not useful for my discussion of the differences between gastric and duodenal ulcer. The appropriate table of the Hammond and Horn study⁴ has the entries:

TABLE 1

	Smoking	Observed	Expected	Ratio
All deaths	None	1,644	—	1.00
	Cigarette	7,316	4,651	1.57
	Other	2,916	2,563	1.14
Gastric ulcer	None	0	—	1.00
	Cigarette	46	0	Inf.
	Other	5	0	Inf.
Duodenal ulcer	None	8	—	1.00
	Cigarette	54	25	2.16
	Other	11	12	0.92

By "None" is meant men who never smoked; by "Cigarette," those with a history of regular cigarette smoking, whether or not they smoked pipes or cigars in addition; by "Other" is meant those who smoked but never cigarettes regularly.

It is noted that those who never smoked never died of gastric ulcer; this gave a zero under "Expected" to go into the denominator of the expected deaths of smokers and accounts for the entry "Inf." (for infinity) in the ratio column. It is difficult to believe that with a much larger sample one would continue to find that non-smokers never died of gastric ulcer, though the rate might be very small. The 46

cigarette smokers who died of gastric ulcer constitute enough to be really significant statistically; but the 5 "other" smokers are too few to be significant and so the infinite ratio is not.⁵

Turning to duodenal ulcer, we find 8 deaths among nonsmokers, which is significantly greater than 0 as found for gastric in the same population. The figure of 54 for cigarette smokers is undoubtedly significantly greater than the 25 expected; indeed, of all the 14 different diseases or disease groups tabulated by Hammond and Horn in their Table 1, the mortality ratio of 2.16 for cigarette smokers from duodenal ulcer is the greatest except only that for nonmalignant pulmonary diseases (for which it is 2.85).

As a recorded cause of death both gastric and duodenal ulcer are rare; in the Hammond and Horn series, the former is $1/233$, the latter is $1/163$, and both together are $1/96$ in the age range 50 to 74. For Scotland in 1943 for the same age group, they were respectively $1/112$, $1/97$, $1/49$, roughly twice as large. These figures are for males; those for females would be very different.

Conclusion.—Based on death statistics, the different sex ratio, the different age distribution, and the different reaction to smoking make the epidemiology of gastric and duodenal ulcer different. At the very least, it would be desirable that in treating peptic ulcer gastric and duodenal ulcer be separated until such time as it may be seen whether the separation is really necessary.

¹ Yule, G. U., *An Introduction to the Theory of Statistics* (6th ed., 1922), p. 372 in Supplement 3 and p. 217, formula (12), in chapter 11.

² That the deaths should be increasing is natural in a decade in which population has been increasing, but increases have not been found uniformly in Massachusetts or New York for which the trend equations are:

Males	Gastric	$135.4 - 2.01 t$	Duodenal	$164.2 - 1.56 t$
Females	"	$49.2 + 3.10 t$	"	$45.7 + 2.36 t$
Males	"	$459.1 - 0.90 t$	"	$482.8 + 12.36 t$
Females	"	$157.9 + 11.67 t$	"	$110.7 + 8.42 t$

The statement of Cecil and Loeb that men are afflicted with gastric and duodenal ulcer about four times more frequently than women is somewhat too high for the deaths in these two states and the whole United States.

³ To get numbers of adequate size, ages were grouped into nine divisions: 0-4, 5-24, 25-34, and by decades to 75-84, finally 85 and up. The χ^2 values for each of the four years were above 20, the $P = 0.01$ point for 8 degrees of freedom, and the values for the 2×2 tables were also all above 6, the $P = 0.01$ point, when the split was made at age 65, except for the year 1960, which was not significant when split there but was below the $P = 0.05$ point when split at 75 or 55.

⁴ Hammond, E. C., and D. Horn, *J. Am. Med. Assoc.*, 166, 1159-1308, Table 1, p. 1295. Doll and Hill and Dorn did not divide peptic ulcer into its two components.

⁵ I am not sure how one should compare an observed with a calculated case; but if one sets up a 2×2 table comparing 0 and 5 with 1,644 and 2,563 by χ^2 with Yates' correction one finds $P = 0.18$. If one uses the Fisher-Yates series, one gets 0.084 on one tail and 0.078 on the other, making 0.162 to compare with 0.18.