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• EDITORIAL •

Why a *World Journal of Gastroenterology*?

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When a new medical journal is launched, the reaction is frequent: Why? Do we have already so much to read that we feel overwhelmed? But, the litmus test of a good new journal is: Does it find its way into the reading time of physicians and medical scientists? The new *World Journal of Gastroenterology* has the opportunity to pass that litmus test.

We already have excellent journals of gastroenterology. All have originated as local publications. Some have reached an international status because of the quality of the published materials. Clear examples in the Western world are journals originated in Great Britain, Scandinavia and the United States of America. But they all keep their original flavor which permeates their published materials and reflects mostly the experience and the interest of physicians in the countries they represent.

Gastroenterologists, as most clinicians, tend to draw conclusions from their own experience, which they tend to generalize to "the world". That experience represents the pattern of diseases in their community. But gastrointestinal diseases display radically different patterns in different populations. In the case of cancer, for instance, the incidence of cancers of the colon, liver, biliary system, and stomach displayed rates in some populations that were several times higher than in other populations, as regularly published and illustrated by the International Agency for Research on Cancer[1].

The phenomenon is well illustrated by gastric cancer and its precursor lesions. Their morphologic characteristics were first masterfully described and illustrated by European pioneers such as Faber, Fenwick, Magnus and Kupfer approximately a century ago[2-5]. In those days pernicious anemia was a major medical problem in Europe and was, with good reasons, linked to gastric carcinogenesis. At the present time pernicious anemia has drastically decreased in frequency perhaps due to improved nutrition and sanitation. However, the genes for the predisposition to the syndrome remain in the population. The type of gastric adenocarcinoma originally described in association with pernicious anemia (the papillary type, located in the corpus) has become very rare[6]. But it is entirely possible that the genes that predispose to pernicious anemia in one set of environmental conditions may manifest themselves as a different disease in another set of conditions. It has been suggested in populations susceptible to pernicious anemia, the initial trigger for chronic gastritis may be *Helicobacter pylori* infection. In such populations gastritis may be severe in the corpus leading to atrophy of the oxyntic mucosa[7].

Most clinicians attending only populations of non-European extraction have never seen a case of pernicious anemia. The genes linked to that disease are either rare or not present in their population and gastritis associated with *Helicobacter pylori* in their patients is multifocal but antral predominant, with minimal or absent corpus involvement. Some medical writers concentrated on corpus atrophy as a cancer precursor and ignore the gastric antrum[8]. They might not appreciate that outside Europe, most gastric cancer precursors were predominantly in the antrum, not in the corpus.

Some publications insist that the high cancer risk gastritis phenotype depends on the grade and activity of gastritis in the corpus. The general experience presently showed that the antrum and the antrum-corpus transition zones (mostly the area of the incisura) were the sites of the most advanced lesions, including intestinal metaplasia, dysplasia and carcinoma[9].

The Jarvi-Lauren classification of tumors as "intestinal" or "diffuse" has been challenged. Some reports have concluded that gastric carcinomas may arise as "gastric type" and later convert to a mixed type, expressing gastric and intestinal mucins. It has been suggested that stem cells, from which carcinomas are supposed to arise, are "primarily gastric type" (meaning they encode for gastric mucins only)[10]. Normal stem cells have a minimal amount of acid (intestinal) mucins, indicating repressed genes and explaining their multi-potential characteristics[11]. Obviously the ultimate mechanism of carcinogenesis is not well understood. An attractive hypotheses has been recently discussed by Kirchner *et al.*[12]. They presented scientific evidence in support of a mechanism of carcinogenesis based on atrophy (loss of differentiated cells) followed by re-differentiation of stem cells, which may be abnormal. This would explain the carcinogenic process of the gastric and cardiac mucosae. After atrophy, the so-called complete intestinal metaplasia expresses preferentially small intestinal (sialic) mucins. Later the so called "incomplete" metaplasia appears and expresses several types of mucins, including gastric MUC-5AC and MUC-6, small intestinal MUC-2 and large intestinal DAS-1[13]. These findings do not support gastric carcinoma classification based on mucin expressions as "gastric", "intestinal" or "mixed". Mucins expressed by pre-neoplastic and neoplastic cells represent abnormal re-differentiation which is not a permanent but rather a represent dynamic expression of mucin genes present in stem cells.

We hope that the *World Journal of Gastroenterology* will minimize the "provincial" bias and inspire the authors to be less dogmatic and more eclectic. We also hope that future authors adopt some of the basic teachings of epidemiology. For example, (1) Disease patterns are strongly influenced by the geographic and demographic characteristics of the populations under study. The local experience may not be applicable to all populations. Frequently, more than one demographic group share the same geography, comparison of such groups offers opportunities for etiologic research. (2) Disease frequency determines population risk and there are clear rules to assign causality. As an example, cancer frequency is often measured in the number of cases per 100 000 populations. Invasive gastric carcinoma is the final stage of a prolonged precancerous process involving chronic gastritis, atrophy, metaplasia and dysplasia. As in precancerous processes in other organs, the earlier stages are very frequent but less predictive of eventual neoplastic outcomes. Later stages have a lower prevalence in the population but are better indicators of cancer risk. Let us

remember that the skin of all people is exposed to the effects of sun rays which may lead to several degrees of actinic damage. But very few develop skin cancer. Large cohorts observed for many years may provide more valid data than small cohorts followed-up for a few years. Large cohorts have been reported in Finland, Yugoslavia and Japan[14-16]. (3) As in all medical sciences, epidemiologic observations may be biased. But epidemiologists have figured out how to deal with bias. Causal *vs* non-causal associations are distinguished by epidemiologic criteria such as strength, consistency, temporality, and plausibility of the associations.

Recent advances in medicine and biology have made it possible to depend less on experimental animals to test causality. Molecular changes can be traced in human cells, tissues and fluids, but molecular techniques are not an end in themselves. Clinicians and medical scientists should remember that these new techniques are merely tools to explore causality in human beings. The new science of molecular epidemiology in some way should make molecular biologists use the epidemiologic techniques to analyze their findings. Similarly, classical epidemiologists need to become acquainted with the new powerful tools provided by molecular biologists. More than ever, multidisciplinary teams are needed to make real progresses in our understanding of the complex processes of carcinogenesis.

REFERENCES

1 **Parkin DM**, Whelan S, Ferlay S. Cancer incidence in five continents. Vol. VII. International Agency for Research on Cancer Publication. *Lyon, France* 1993: 143
2 **Faber K**, Block CE. Uber die pathologischen Verenderungen am digestion tractus bei die perniciosen anemia und ulcer die Sogennante. *Dermat Z Klin Med* 1900; **40**: 98
3 **Fenwick S**. On atrophy of the stomach. *Lancet* 1870; **2**: 78-80
4 **Kupfer C**. Festschrift. *Arz Verein Munch* 1883: 7
5 **Magnus HA**. A re-assessment of the gastric lesion in pernicious anaemia. *J Clin Path* 1958; **11**: 289-295
6 **Elsborg L**, Mosbech J. Pernicious anemia as a risk factor in gastric cancer. *Acta Medica Scandinavica* 1979; **206**: 315-318
7 **Carmel R**, Perez-Perez G, Blaser MJ. *Helicobacter pylori* infection and food cobalamine malabsorption. *Dig Dis Sci* 1994; **39**: 309-314
8 **Meining A**, Morgner A, Miehlke S, Bayerdorffer E, Stolte M. Atrophy-metaplasia-dysplasia-carcinoma sequence in the stomach: a reality or merely a hypotheses? *Best Pract Res Clin Gastroenterol* 2001; **15**: 983-998
9 **Rugge M**, Cassaro M, Pennelli G. Atrophic gastritis: pathology and endoscopy in the reversibility assessment. *Gut* 2003; **52**: 1387-1388
10 **Endoh Y**, Sakata K, Tamura G, Ohmura K, Ajioka Y, Watanabe H, Motoyama T. Cellular phenotypes of differentiated type adenocarcinoma and precancerous lesions of the stomach are dependent on the genetic path ways. *J Path* 2000; **191**: 257-263
11 **Jass JR**, Filipe MI. The mucin profiles of normal gastric mucosa, intestinal metaplasia and its variants and gastric carcinoma. *Histochem J* 1981; **13**: 931-939
12 **Kirchner T,** Muller S, Hattori T, Mukaisyo K, Papadopoulos T, Brabletz T, Jung A. Metaplasia, intraepithelial neoplasia and early cancer of the stomach are related to dedifferentiated epithelial cells defined by cytokeration - 7 expressions in gastritis. *Virchow's Arch* 2001; **439**: 512-522
13 **Piazuelo MB**, Haque S, Delgado A. Phenotypic differences between esophageal and gastric intestinal metaplasia. *Mod Pathol* 2004; **19**: 62-74
14 **Siurala M**, Isokoski M, Varis K. Prevalence of gastritis in a rural population. *Scand J Gastroenterol* 1968; **3**: 211-223
15 **Filipe MI**, Munoz N, Matko I, Kato I, Pompe-Kirn V, Jutersek A, Teuchmann S, Benz M, Prijon T. Intestinal metaplasia types and the risk of gastric cancer: a cohort study in Slovenia. *In J Cancer* 1994; **57**: 324-329
16 **Ohata H**, Kitauchi S, Yoshimura N, Mugitani K, Iwane M, Nakamura H, Yoshikawa A, Yanaoka K, Arii K, Tamai H, Shimizu Y, Takeshita T, Mohara O, Ichinose M. Progression of chronic atrophic gastritis associated with *Helicobacter pylori* infection increases risk of gastric cancer. *Int J Cancer* 2004; **109**: 138-143

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