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Early Diagnosis of Colorectal Cancer: A Preventive Task in Occupational Health

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Abstract
Morbidity of colorectal cancer is still accreting; therefore in 2003 a total of 57000 patients fell ill and about 28000 died due to colorectal carcinoma. According to the etiology, many different factors are currently in discussion. However, as in about 25-30% of the cases familial clustering can be observed one of the most probable might be the genetic predisposition. Nevertheless only in 3% of all cases this predisposition is also scientifically assured. The high average age of manifestation raised the question if there might be also an occupational relationship for colorectal carcinoma in tense of an occupational disease. Therefore there is sight for occupational health to contribute to early diagnosis of colorectal carcinoma within the scope of routine check-up, health management and research of occupational diseases.

Key words: Colorectal Carcinoma, Occupational Medicine, Prevention, Occupational Disease

Incidence and Life-time Risk

In Germany, the incidence of colorectal cancer has increased since the 1970's. The incidence of colon carcinoma standardized over all ages for the European population in 1970 was doubled for men from 24 to 44/100.000 residents in the Saarland in 1993. Since the beginning of the 1990's these numbers remain static and respectively slightly decreased [1]. In the Saarland, the only federal state regulating a cancer register since 1967, the incidence of colon carcinoma was 42 for the male and 30 per 100.000 residents for the female population in 2003.

However, the increase of incidence of rectal carcinoma was slower. In comparing the years 1970 and 1999, an incidence of 25 and respectively 29 per 100.000 male residents of the European population was registered whereas for women the incidence of rectal carcinoma was 14 in1970 respectively 29 per 100.000 European residents in 1999 [2].

In comparison to the rest of the EU-countries and the U.S., Germany presents the highest incidence of intestinal cancer for the male as well as for the female population. Compared with the standardised occurrence of intestinal cancer over all ages per 100.000 residents, Germany ranks at the top of the European countries [1].

The lifetime risk to develop intestinal cancer in Germany is 6% whereas mainly the elderly population is affected [2] (Fig. 1). The mean age of manifestation is 67 years for men, and 72 years for women. More than 80% of all cases of intestinal cancer occur in persons older than 60 years (colon cancer 86%, rectal carcinoma 76%).

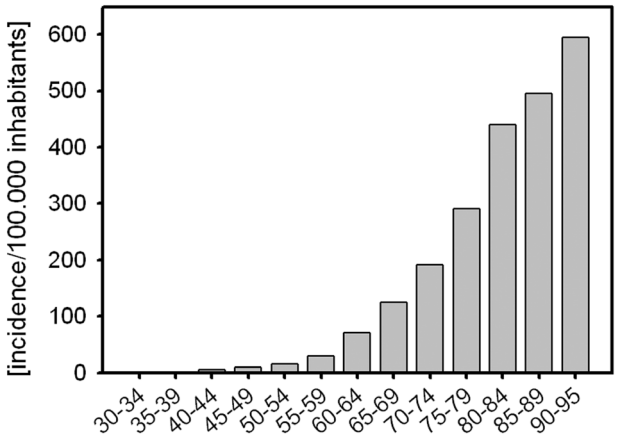

Fig. 1. Age distribution pattern of colorectal cancer: Incidence of colorectal cancer per 10000 inhabitants in the Saarland (state in Germany) from 1990-1999.

Already in 1990, a yearly incidence rate of 27.000 in men, including 15.000 cases of colon carcinoma, and of 3.0000 in women, including 190.000 cases of colon carcinoma, had to be assumed in Germany [3].

In 1999, 57.000 patients contracted a colorectal carcinoma, whereas 29.800 patients died due to it in Germany (consensus conference colorectal carcinoma 2004).

Thus, colorectal cancer accounting for 16.7% presented the second common cancer in women follow-

ing breast cancer, and respectively accounting for 16.0% in men presenting the third common cancer type of incidence following prostate cancer and bronchial carcinoma.

Mortality and Survival Rates

Considering these numbers, colorectal cancer presents the second common cause of death due to cancer disorders in Germany in men and women. In the year 2000, 9.000 men and 1.000 women died of colon cancer, whereas 4.500 men and 4.000 women died of rectal cancer 4. In the same time period, 29.000 men died of bronchial carcinoma and 18.000 women died of breast cancer. The standardised mortality rate over all ages of colorectal and anal carcinoma accounted for 32.1 respectively 23.4/100.000 residents in the male respectively female population between 1996 and 1998.

Regarding the incidence as well as the mortality rate, both parameters were worse for the male population. In contrast to the continuously increasing incidence rate of colon carcinoma the strong increase of mortality was followed by a trend of reconversion with consecutively decreasing mortality in men and women after World War II. [5]. However, the mortality due to colorectal carcinoma is still increasing due to the accretive age of the total population.

For men and women with the diagnosis of intestinal cancer the loss of life expectancy ranged at a mean of 6 years. Patients older than 70 years present with the worst 5 year survival rate [6].

The survival rate strongly depends on the stage of disease at the time point of diagnosis accounting for 80% in case of local limited colon carcinoma (stage I and II), for 60% in case of regional circumscribed tumour progression (stage III) and for >10% in the stage of metastases (stage IV) [7]. Six years after diagnosis the prospect of survival and respectively the mortality do not significantly differ from these of the general population.

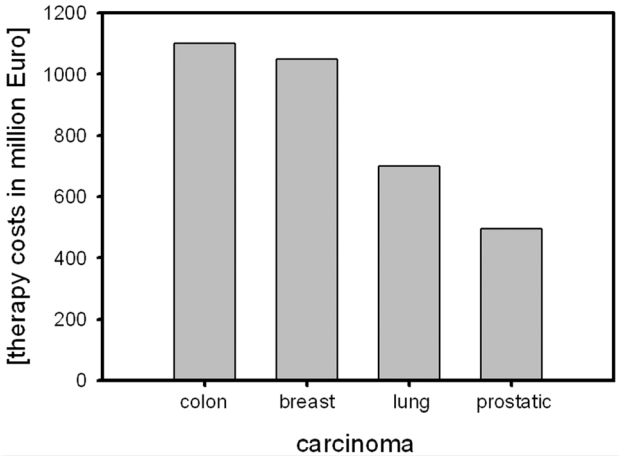

Fig. 2. Estimated direct therapy costs for different cancer types in the year 1994 (Source: Federal German statistics office: health report for Germany in 1998).

Patients suffering from intestinal cancer between 1985 and 1988 presented with a loss of life expectancy of 43% in women and of 46% in men, thus the mortality has significantly improved over the years.

The estimated portion of cured patients over 50% in the 1980s leads to the conclusion that an improvement of the 1-2 year as well as of the 10 year survival rate resulted from the enrolment of patients who were early diagnosed in stage I. In addition colorectal carcinoma stands for an important economical factor because it presents the cancer out of the four most common cancer types leading to the highest direct cost of treatment for the health insurance companies (see Fig. 2).

Etiology and Familial Predisposition

The etiology of the colorectal carcinoma is of complex nature assuming lifestyle-associated as well as hereditary factors and is currently one of the major topics in science.

Following the results of the consensus conference in Bochum, one presumes that overweight over a BMI of 25kg/m^2 presents a definite risk factor (consensus conference colorectal cancer, 2004). The question whether this factor is additionally influenced by reduced physical activity remains unclear [8]. The opinion that physical activity might reduce the risk is based on the fact that bowel motility is pushed by physical activity and the presence of faecal matters in the colon and rectum is shortened due to a higher defecation frequency assuming a reduced impact time of concentrated toxic substances on the colon mucosa [9].

Regarding the nutrition factors, a high proportion of dietary fibres is correlated with a high protective effect. Although various and controversial studies exist, one supposes the protective effect with an essential amount of dietary fibres of at least 30 grams with more evidence of the protective effect for vegetables than fruit [10]. However, it remains unclear on which component the protective effects depends regarding cellulose, flavonoids or anthocyanin. In countries with a high proportion of the daily nutrition accounting for white meat of poultry or fish, a lower frequency of colorectal cancer is present. Thus, it might be assumed that in countries mainly consuming „red“ meat, such as beef, pork or veil, an increase of the frequency might occur, even though no study exists evidently proving a distinct protective effect of fish. Also a special preparation of meat or fish seems to play an additional role.

Not only concerning various nutrition components, such as folic acid or calcium as well as micro-nutrition elements and vitamins, no assured data exist for the proof of a protective effect, but also for pharmaceuticals such as acetylsalicylic acid or hormones for women 4.

In 20 to 25% of the cases a familial risk is considered, whereas in only 1-5% of the cases additional hereditary factors can be included. In case of the hamartomatous polyposis syndrome (<0.1%) and the familial adenomatous polyposis coli (<1%), at a median of 36 years all patients with uncountable adenomatous polyps develop a carcinoma without any exception.

The greatest part of hereditary colon carcinoma owns the HNPPC (hereditary Non-Polyposis Carcinoma) -Syndrome with a rate of up to 3% [11, 12] with a manifestation of rather mucinous carcinoma in the right colon at a median of 46 years 13. Also inflammatory bowel disorders with increased inflammatory activity increase the risk of intestinal cancer. A patient with 20 years history of ulcerative colitis with consecutive pancolitis has a cumulative risk of cancer development of 8.5%, respectively of 17.8% after 30 years. For patients suffering from Crohn`s disease, a 3.5 to 7 times higher risk of cancer development compared to the rest population is considered [14, 15]. Colon carcinoma underlies an adenoma-carcinoma sequence and most likely develops from intestinal polyps [16, 17], whereas in over 90% an adenocarcinoma results. In biopsies from patients older than 60 years, 30% showed already existing polyps [17]. The cancer risk hereby depends on the polyp type, whereas tubulous and villous as well as mixed types can be differentiated. Proportionally to the polyp size the likelihood for degeneration increases as well as the risk to suffer from colorectal carcinoma [4].

Tasks in Occupational Medicine

Traditionally, lung as well as skin disorders have been the primary focus of scientific work in occupational medicine.

The reasons are that due to operational conditions and production processes, mostly pneumologists and dermatologists were working in the field of occupational medicine and that the main focus of pneumology and dermatology were easy to examine whereas the fiberoptics technology for the examination of the gastrointestinal tract is only available since the mid 1960s [18].

Due to increasing accumulation of work disability in the health insurance statistics, gastrointestinal disorders found their way into occupational medicine and are of increasing importance. For work disability cases, disorders of the gastrointestinal tract rank at third place, whereas for the number of treated days the fourth rank has been taken in account.

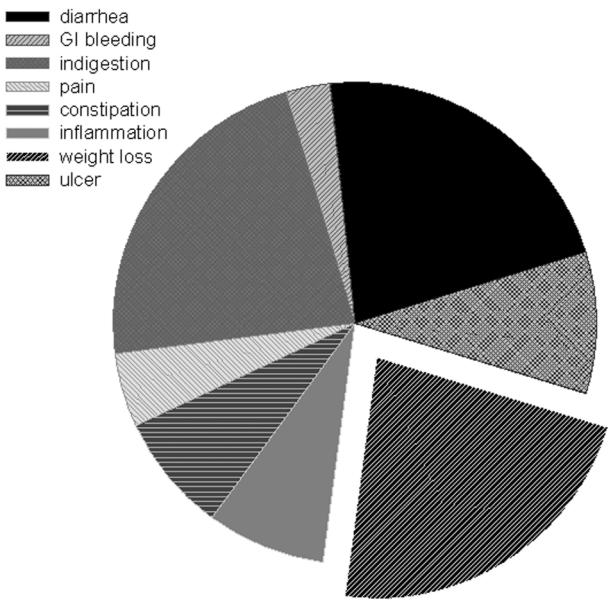

Fig. 3. Pattern of gastrointestinal symptoms in occupational diseases.

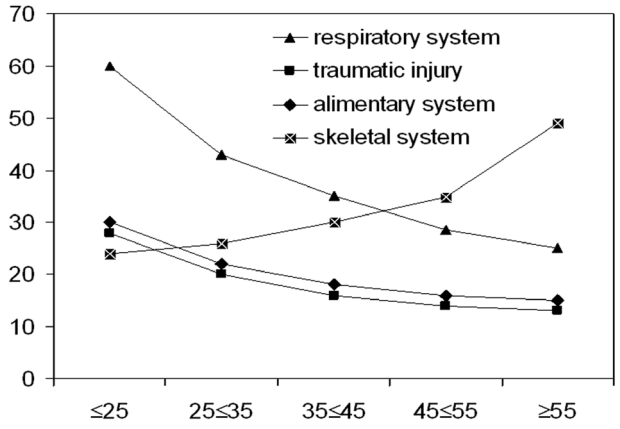

Fig. 4. Cases of work inability reported by AOK in 2001 per 100 obligatory members.

Although gastrointestinal symptoms, especially in correlation with occupational disorders, are not to be neglected, scientific technical literature published by law are not desirable and contain insufficient information [19]. Reclusively, the terms of the gastrointestinal syndromes' spectrum of the singular occupational disorders are partially very sweeping and unspecific 20. Loss of weight, inflammation, diarrhoea, constipation, pain and unspecific digestive disorders of various degree are considered symptoms regarding occupational disorders [21-23]. However, the issue of the symptom gastrointestinal bleeding is not addressed at all. For the development of chronic symptoms, the lower gastrointestinal tract seems to be more responsible, whereas the incidence for acute symptoms is higher in the upper gastrointestinal tract. 22 of the 29 group I occupational disorders (disorders caused by basal metal, metalloids, or other chemical compounds) are associated with the report of gastrointestinal symptoms accounting for 75.7% related to all existing occupational disorders [24]. The causation for the greatest part of chronic symptoms is in 48.3% of all occupational disorders localised in the lower gastrointestinal tract leading to a different incidence of symptoms: 1 symptom is present in 6, 2-3 symptoms are apparent in 13, 4-5 symptoms appear in 6 and more than 6 symptoms are present in 2 different occupational disorders. In 32% of occupational disorders one gastrointestinal symptoms is present, in 46% of the cases 2-3 symptoms appear and in approximately 30% 1-3 symptoms can be present, whereas the incidence of symptoms decreases in the direction to the colon [24].

The characteristic of colorectal carcinoma lies within the fact that patients do not present with any kind of problems. The development and the progression of colorectal polyps usually process totally asymptomatically. Concerning long pedunculated polyps sometimes non-specific vesicant problems can be defined due to

traction on the polyps' base. Usually the development is missed by diagnostics and only in the case of a in the lower colon or rectum localised polyp causing a distinct anal bleeding. Polyps with a localisation in the upper gastrointestinal tract are usually only detected by the performance of the faecal occult blood test with a specificity of 97.6%, because the colon polyp mucosa might bleed intermittingly and more frequently than normal colon mucosa [25]. Unspecific symptoms such as changing defecation or pain are not informative [24].

Role of Potential and Proven Carcinogens

The newly established occupational disorders regulation as well as the list for dangerous substances lists a number of substances which themselves or via metabolites can be potentially effective or are proven to be carcinogenic. They are used for many technical production processes, but are also used in trade occupations [24]. Many of these substances are of exhalable character at normal processing temperatures, thus can be incorporated inhalational. Despite protective mechanisms of the nasopharyngeal mucosa, these substances are also absorbed ingestively via clearing effects by swallowing. Thus, toxic and carcinogenic substances are incorporated into the gastrointestinal tract presenting the largest boundary layer of the human organism. Gastrointestinal problems are brought up earlier in occupational life and lead to consecutive nonproductive work time. It is a long known and valid insight that a tumorous disease not necessarily manifests in the same tissue structures, where the carcinogenic substances were incorporated [26]. This fact is documented for inhaled asbestos fibres leading to pleural mesothelioma as well as for organic solvent like benzene being absorbed via lung and skin, leading to myelodysplastic disorders [27, 28].

Tumour induction can take place in the absorbing tissues (benzopyrene) themselves on the one hand, and on the other hand via displacement in other tissues and local accumulation (e.g. benzenehexachloride [29]). Concerning the exact resorptive mechanisms of the gastrointestinal tract for single substances, scientific evidence is still lacking.

However, several theories for the absorption of nutriments, vitamins or heavy metals like iron passing the intestinal epithelia via active or passive mechanisms exist. It is largely ensured that complex organic and anorganic compounds like halogenated aromatic chlorinated hydrocarbon more easily permeate the cellular membrane due to the high lipid solubility, although the question concerning polarity of compounds in correlation with the epithelial structure remains unclear [24]. The retention period of carcinogenic substances in the cell is not clarified as well as the question remains to be answered, whether the metabolism of potentially or proven carcinogenic substances might already begin in the epithelial cell of the intestines. In this context, the substance class of epoxy resins has to be mentioned, which plays an important role in numerous manufacturing processes and is currently scientific topic in cancer research [30].

Occupational Disease after Exposure

In Germany in 1997, 1739 persons died of industrial or way accidents [31], in the same year 2071 persons died of occupational diseases (Hauptverband der gewerblichen Berufsgenossenschaften 1999). In 1116 of these cases, the fatal diagnosis was a cancer disease. Correlating these deaths to the whole number of insured patients having died of an occupational disease, 53.9% of all insured workers died of cancer 3. Taking into account, that in Germany in the same year from 884.588 deaths 24.1% were due to cancer, the future discussion in occupational medicine has to elucidate whether a higher rate cancer due to occupational reasons remains unrecognized [31]. Of course, recognition in occupational medicine is aggravated as numerous disorders present with a typical time lag; in most cases a long time after the working life has been finished.

In this context unfortunately the daily clinical routine shows that especially in the elderly population for anamnesis rarely questions concerning the patient's occupational life and potential prior exposition to hazards etc. are asked. Moreover, a nationwide cancer register with the registration of tumour diseases was scarcely established between 1995 and 1999. Since the law for occupational safety is only obtained since 1973, an inadequate area of insufficient acquisition of occupational exposure prevails for the entire period before 1973 as well as for the first 10 to 15 years after. Especially disorders with long latency complicate the expert survey regarding the causality of a cancer disease. The new BKV contains explicit reference to cancer diseases in only 7 disorders. As a matter of fact, in 15 occupational disorders cancer diseases occur, whereas an approval of tumour disorders according to paragraph 9, article 2 of the German VIIth Code of Social Law is not implied. Cancer disorders have continuously increased for the statistics of the social insurances, especially after the German reunion with the beginning of the 1990s due to exposure to bismuth and uranium ores mining in the former German Democratic Republic.

Nowadays, every fourth new annuity case is due to a cancer disorder (see Fig. 5) [31]. The majority of accredited cancer diseases is recruited from occupational disorder with the major focus on ionizing radiation – 2402(OD), asbestos lung cancer – 4104(OD) and asbestos mesothelioma –4105(OD), whereas in the time period between 1978 and 1997 a proportion of 4415 diseases of the total 14337 cancer diseases were determined by other noxious matters such as chromium, arsenic, aromatic amines, benzene and wood dust, to name the most common. Explicitly, regarding OC 1310 including disorders of halogenated alkyl- or alkylaryl-oxides the appearance of carcinoma in the gastrointestinal tract was proven and accredited [31].

It is necessarily supposable that other halogenated chlorinated hydrocarbon producing similar metabolites with their metabolism as appearing in metabolism of substances of OD 1310 induce carcinoma in the lower gastrointestinal tract, in case of sufficient examinations. Surprisingly, death of OD 4105 (asbestos induced mesothelioma of the pleura, the peri-

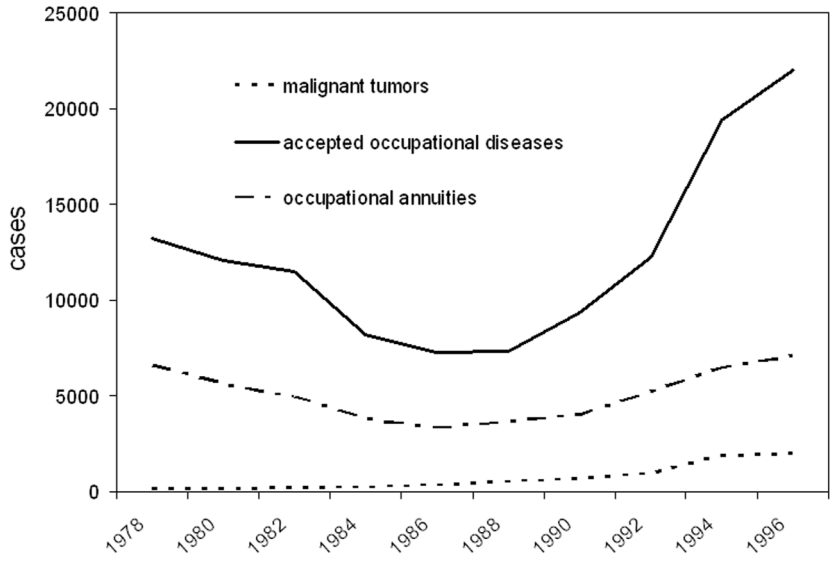

Fig. 5. Development of occupationally caused cases of cancer in comparison to accredited occupational diseases (occupationally caused cancer diseases, HVBG 1999).

toneum as well as of the pericardium) includes 198 cases of peritoneal mesothelioma. So far, scientific proof of the diversion of asbestos fibres into the peritoneum is still lacking in the current literature. But it is supposable that at least a portion of fibres of swallowed asbestos dust and consecutive intestinal absorption is the reason. In this context an actual American work suggests, that colorectal cancer risk is elevated among men occupationally exposed to asbestos, especially those with evidence of nonmalignant asbestos-associated radiographic changes of the lung 32. Moreover, there are at least two cases of pericardial mesothelioma documented, which most definitely developed due to the diversion of the asbestos fibres via the lymphatic system into the adjacent pleura and lung [31].

However, the carcinogenic effect mechanism of oak and beech dust on the mucosa of the main nasal cave and the adjacent sinuses remains unclear. In case of development of a carcinoma due to the coverage of the epithelia with oak and beech dust, it is thus supposable that such a coverage in the gastrointestinal tract with longer exposure times and greater interfaces also may lead to the development of carcinoma following the diversion of corresponding dust [24].

Conclusion

The inquiry of reports of suspected occupational disease shows that nowadays still disorders of lung, skin, ear and spine are in the main focus of occupational medicine. In contrast, the report of suspected occupational caused colorectal cancer presents an absolute rarity.

Due to long latency of carcinoma and the late incidence of the disease, most likely fateful lapse is accused. Although the genesis of sporadic colorectal carcinoma (approximately in 70% of all cases) remains scientifically still not clarified, a correlation with occupational factors is usually not considered [4].

Regarding several noxious matters, which are already accredited in the OD-system, an induction of colorectal carcinoma is already scientifically reasonable. For numerous occupational diseases a possible gastrointestinal symptomatology needs to be explored as well as the etiological aspect has to be considered. The actual unequal distribution pattern of occupational cancer diseases is most likely still reasoned by the previous diagnostics and emphasis shift.

Therefore most likely a significant proportion of cancer patients is mistakenly excluded from insurance law appreciation. Thus, regarding prevention and early diagnosis of colorectal carcinoma it is not only our duty in occupational medicine to minimize risk factors such as overweight, dietary fibre reduced nutrition and nicotine abuse within the scope of corresponding health promotion and training of co-workers, but also to register an occupational anamnesis of possible noxious and carcinogenic matters.

It is necessarily supposable that with an increasing number of reports of occupationally reasonable colorectal cancer also an augmented accreditation and scientific refurbishment in respect to etiology might result.

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