

HISTORICAL PERSPECTIVES IN OCCUPATIONAL MEDICINE

Changing Attitudes and Opinions Regarding Asbestos and Cancer 1934–1965

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Literature published in the years 1934–1965 was reviewed to determine attitudes and opinions of scientists as to whether asbestos is a cause of cancer. In Germany, the issue was decided in 1943 when the government decreed that lung cancer, when associated with asbestosis (of any degree), was an occupational disease. In the United States, however, there was no consensus on the issue until 1964. Opinions of scientists over a 22 year period are shown and the contributions of various cultural, social, economic and political factors to these opinions are discussed. A lack of experimental and epidemiological evidence played a major role in delaying a consensus. Other important factors included a rejection of science conducted outside of the U.S. during this period, particularly a rejection of German scientific thought during and after WWII, and a rejection of clinical evidence in favor of epidemiological investigations. Individual writers rarely changed their minds on the subject of asbestos as a cause of cancer.

Key words: epidemiology, mesothelioma, lung cancer, asbestosis, literature review, history of medicine

INTRODUCTION

Observations on disease in human populations have made important contributions to our knowledge about causal factors in disease. It is tempting to ask, however, why it took so long to discover things that are today so obviously true. How could we have long missed the association between cigarette smoking and lung cancer, for example. The answer must lie, in part, in what data were available, how data were interpreted by medical observers, and what factors influenced these interpretations. Clearly, some of these interpretations must have been wrong, and if the reasons for

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these wrong interpretations were known perhaps this would ever so slightly accelerate scientific progress in the future.

An excellent example of a costly delay in arriving at a consensus is the situation with regard to asbestos. Why did it take so long to recognize the association between asbestos and lung cancer? How was it discovered? Who contributed to the discovery, and who detracted? What role did the various health disciplines play in arriving at a final consensus? What was the evidence at various points in time and how was it interpreted? Clearly, scientific thought does not take place in a cultural, social, economic, or political vacuum. What role did these factors play in arriving at a consensus?

METHODS

In order to see how medical observers viewed the possibility of an association between asbestos and cancer, all of the open literature on asbestos and cancer was examined, from the first article written in 1934 through 1965, when the issue appears to have been settled. First, all of the literature on asbestos and cancer referenced in the *Index Medicus* and elsewhere for the years 1934–1965 was examined. This included building on references in each article found. In addition, every issue of *Lancet*, the *British Medical Journal*, and the *Journal of the American Medical Association* for these years was searched for any editorials or communications which mentioned asbestos and cancer. Also, all available textbooks on occupational medicine, toxicology, and pulmonary cancer were examined. For all foreign-language articles a complete translation was obtained. As a method of summarizing how, at different points in time, the writers were interpreting the literature and observations then available on the subject of asbestos (or asbestosis) and lung cancer, each article was classified as to how the writer or writers felt about the relationship between asbestos and lung cancer as: 1) asbestos definitely causes lung cancer; 2) asbestos possibly causes lung cancer; or 3) the relationship is unproven. For the first two categories, a subdivision was made as to whether it appeared that the writer thought asbestosis must or must not be present for cancer to occur. This classification was made independently by this author and Dr. I.T.T. Higgins, then professor of epidemiology at the University of Michigan. A similar classification was made on articles dealing with mesothelial tumors by only this author. For articles on asbestos and lung cancer there were surprisingly few disagreements. These were worked out by discussion.

The results of this review are presented to demonstrate how opinions differed on the subject of asbestos and cancer, to show how opinions changed or drifted over a 32 year period, and to identify the kind of scientific publications and the kind of writers that contributed most directly to a final consensus. In addition, a narrative is presented on what appear to be the highlights in the progression of scientific thought toward a consensus and on factors that appear to be associated with this progression.

Some of the material presented is from the monograph *Asbestos and Cancer—The First Thirty Years*, privately published by this author in 1980. An early draft of this monograph was the basis for an editorial published by this author in 1978.

CONTEMPORARY OPINIONS

A total of 104 papers or writings were located which dealt with the subject of asbestos and lung cancer and which were published through 1965, the date by which

the association between asbestos and lung cancer seems to have been firmly established. Table I shows how articles dealing with asbestos and lung cancer were classified. This table also indicates the type of article, whether based on animal or human observations, whether the original article was in some language other than English, and whether the author conditioned this opinion on type of asbestos fiber. In a few cases involving negative animal experiments, the writing has been put under the unproven column even though the writer may have personally believed in an association between asbestos and cancer. Usually, however, where original data were presented, the writer's opinion coincided with what the data seem to show. Only the name of the first author is given. Where textbooks had chapters written by other than the author or editor, the name of the textbook author appears in parentheses after the name of the chapter author. Where discussants of articles are referenced, the discussant is referenced and the name of the first author of the article is shown in parentheses. Unsigned editorials are referenced only as "editorial."

The general impression gained from Table I is that opinions shifted fairly rapidly from "unproven" or "possibly causes cancer" to "definitely causes cancer" during the period from the first published observation on lung cancer in 1934 to 1942. Between 1942 and 1956, not much change occurred except perhaps for a few writings that suggested that asbestosis was not necessarily a precursor to asbestos-caused cancer. During this period, many writers remained unconvinced of a relationship and in 1956, there seemed, in fact, to be a retreat from a consensus as to a causal relationship. The period 1957–1963 also seemed to be one of uncertainty with little change in the position of individual writers on the question of whether asbestos is a cause of lung cancer. In fact, most individual writers held firm to their original position on whether asbestos is a cause of cancer. Perhaps this is unfortunate. It does appear true in all of science, however, that it is better to be wrong than to be inconsistent. Textbook writers were among the last to acknowledge a relationship, whereas writers of editorials were among the first. Note, for example, that after 1951, there are no editorials in the unproven column but five textbooks. Articles in a language other than English are indicated by an asterisk. Nearly all of the early articles in the proven column were in German and it is clear that German writers had made up their minds about the relationship between asbestos and lung cancer by 1943.

A total of 61 papers or writings were found that dealt with the subject of malignant mesothelioma and asbestos. Whether asbestosis needed to be present for this cancer to occur was never an issue. Table II classifies articles that deal with mesothelioma as: 1) asbestos definitely causes mesothelioma; 2) asbestos possibly causes mesothelioma; and 3) the relationship is unproven. Included are articles in which the cancer was not recognized as a mesothelioma but in retrospect appears that it was indeed a mesothelioma. Information is coded as in Table I.

Few authors ever expressed doubt about the relationship between malignant mesothelioma and asbestos exposure, and by 1953, the issue seemed to be fairly well resolved. Actually, rare diseases like malignant mesothelioma are relatively easy to identify with occupational exposure, so that many of the problems in linking more common diseases, such as lung cancer, with asbestos exposure did not apply here. Moreover, those who observed mesothelial tumors did not usually demand epidemiological evidence. The main problem was in agreeing that such tumors actually existed and how they should be defined. Until the report by Wagner et al. in 1960,

TABLE I. Opinions of Authors Publishing 1933–1965 Regarding the Causal Relationship Between Asbestos and Lung Cancer*

Year	Definitely causes lung cancer		Possibly causes lung cancer		Unproven
	Without asbestosis	Only after asbestosis	Without asbestosis	Only after asbestosis	
1934					Wood {O}
1935				Lynch {O}	Gloyne {O}
1936				Egbert {O}	Gloyne {O}
1938		†Nordmann {O} †Hornig {O}		†Teleky {R} †Koelsch {R}	Vorwald {O,a} Editorial (1) Editorial (2) Gloyne {T}
1939		†Baader {R}		Klotz {O} †Saupe {O}	Lynch {O} ILO {R} Lanza {T}
1940					Gardner {R}
1941	†Nordmann {O,a}	†Linzbach {O}		†Desmeules {O}	
1942		†Wegelin {R} †Welz {O}		Holleb {O} Heuper {T}	
1943		†Wedler (1) {O} †Wedler (2) {R} †Boemke {O} Hueper {R}		Homberger {O}	Wampler {T}
1946		Hueper (1) {R} Hueper (2) {R}			King {O,a}
1947				Kennaway {O}	†Wegelius {O}
1948		†Saita {R}		Lynch {O} Cureton {O}	Warren {R} Teleky {T}
1949		Merewether {O} LW Smith {R} Wyers {O}		Doig {R}	
1951		Editorial Hueper {R} Owen {O,q} Stoll {O} Tabershaw {R}	Gloyne {O}		Vorwald {O,a} †Behrens {O,a} Sax {T}
1952		Hueper {R} †Werber {O}		†Behrens {R}	WE Smith (1) {R,a} WE Smith (2) {O} Cartier {R} Lanza {R}
1953	Clemmesen {E}	WE Smith {R} Isselbacher {O} †Weiss {O} †Boemke {O}		Lynch {O}	Vorwald {C}
1955	Doll {O} Editorial (1) Editorial (2)	Hunter {q} Knox {C} †Rambola {O,f} †Portigliati, Barbos {O} †Hueper (2) {O} Bonser {O} Merewether {O} Hueper (3) {R}	Breslow {O}	Lynch {O} KW Smith {R,f} †Jacob {O}	Cartier {O} Hueper (1) {O,a}

(continued)

TABLE I. Opinions of Authors Publishing 1933–1965 Regarding the Causal Relationship Between Asbestos and Lung Cancer* (Continued)

Year	Definitely causes lung cancer		Possibly causes lung cancer		Unproven
	Without asbestosis	Only after asbestosis	Without asbestosis	Only after asbestosis	
1956		Weller {T} Hueper {R} †Bohlig {R}		Goldblatt {T} †Francia {O,f} McGee {q}	Rosenblatt {T} Todd {O} Hammond {T} †Bohlig {R}
1957		Jones-Williams {O} Fairhall {T,q} Editorial		O'Donnell {O}	Sax {T} Lynch {O,a}
1958	†Schmähl {O,a,♣}	Goldblatt {R} †Bohlig {O} †Chauvet {O}		Sander {T}	Braun {O} †Bohlig {O}
1959	†Bohlig {O}	DuBois {T} Hueper {T} †Bohme (1) {O} †Bohme (2) {O} Eckardt {T}		†Nordvik {R,f}	
1960	Schepers {T} Gilson {T,f} †Konig {O}			Keal {O} Anderson {O}	Johnstone {T} Dunn {O}
1961		Heard {O} Telischi {O} †Frankel {O} Trimble {C} †Krzymien {R}		†Sczymczykiewicz {R}	Johnstone {C}
1962			†Champeix {O} †DeLaguillaumie {O} Hunter {T}	Cordova {O} †Fingerland {O}	†Danrigal {O}
1963	Mancuso {O}	Leatheart {O} Knowles {O} Walters {O}		†Farina {O}	KW Smith {T}
1964	Doll {O} Elwood {O} Oettle {O} Selikoff {O}	†Noeninckx {O} Buchanan {O,f}		†Navrátil {O} †Kogan {O} Gafafer {T}	Am. College of Chest Physicians {R,f}
1965	Editorial (1) Working Group, UIAC {E}	Dutra {O} Elmes {O} Hinson {R} Jones-Williams {O} Editorial (2) †Anspach {O}	Cauna {O}		Andrews {T,q}

*O, original article (observations, studies, experiments); R, review article; E, editorial; C, communication (letters, etc.); T, textbook or monograph; †, foreign language article (not English); a, animal data; q, quote from other source—no opinion expressed; f, association depends on type of fiber; ♣, sarcoma only. For example author's last name {O,a,f} indicates an original article on an animal study where the author expressed the opinion that the association is dependent on the type of fiber. Where there was more than one author only the first author's name is given. If that author published more than one article in a single year articles are identified by (1), (2), etc.

TABLE II. Opinions of Authors Publishing 1933–1965 Regarding the Causal Relationship Between Asbestos and Mesothelial Tumors*

Year	Definitely causes mesothelioma	Possibly causes mesothelioma	Unproven
1933			Gloyne {O}
1934			Wood {O}
1943	†Wedler (1) {R} †Wedler (2) {O}		
1949		Doig {R}	
1951			†Behrens {O,a}
1952		WE Smith (1) {R}	Cartier {R}
1953	†Weiss {O}		
1954	†Leicher {O}		
1955		Bonser {O}	
1956		†Bohlig {R}	
1958		†Van der Schoot {O}	
1960	Gilson {T,f} †Konig {O}	Keal {O} Wagner {O} Schepers {T,f}	
1961	Sleggs {O} †Frankel {O}	Heard {O}	Knox {C}
1962	McNulty {O,f} Thompson {O} Wagner {O,a} McCaughey {C} Enticknap {C}	Smithers {C} Hunter {T}	
1963	Smithers {R,f} Mancuso {O} Walters {R} Thompson {C} Lawson (1) {C} Lawson (2) {C}	Knowles {O} Thompson	
1964	Buchanan {O,f} Enticknap {O} Hourihane {O} †Noeninckx {O} Oettle {O} Owen {O} WE Smith {O,a}	Gafafer {T} Murray {R,f} Elwood {O,f} Fowler {O} Selikoff {O} Editorial {f}	Am. College of Chest Physicians {R,f}
1965	Dutra {O,q} Elmes {O} Hinson {R} Selikoff {O} WE Smith {O,a,f} Steel {O} †Anspach {O} Editorial (1) Editorial (2) {f}		

*See Table I for explanations of symbols and style.

these cancers were not a major focus of research. Table II shows that a flood of articles followed the appearance of the paper by Wagner et al., and in 1965 not a single writer expressed doubts about the relationship. Many did condition their opinions on the type of fiber, however, believing that crocidolite asbestos was the type of asbestos most likely to be related to mesothelioma.

LITERATURE HIGHLIGHTS

The earliest recorded observation on lung cancer was a report by Wood and Gloyne in England in 1934. They reported two cases of lung carcinoma seen at autopsy in 53 cases of asbestosis. In 1935, Gloyne gave a complete description of these two cases. Also in 1935, Lynch and Smith reported a case of lung cancer in an asbestosis case from the U.S., and in 1936, Egbert and Geiger also reported such a case from the U.S. In 1938, in Germany, Nordmann added two cases of lung cancer in two cases of asbestosis, making a total of six, and concluded, "A cause-effect correlation must be present here, even if I had been the only observer. We are indeed facing an occupational cancer which affects asbestos workers." Several German writers quickly accepted Nordmann's views. In 1941 they were reinforced by an animal study in which Nordmann and Sorge reported pulmonary carcinomas in two white mice as the result of asbestos dust inhalation. Other German writers considered this the experimental evidence needed for proof, and gave Nordmann credit for discovering the relationship between asbestos and lung cancer. In 1943, the German government issued a decree declaring cancer of the lung, when associated with asbestosis (of any degree), to be an occupational disease (Reichsgesetzblatt I, P. 85, January 25, 1943). A similar decree was issued by the West German government in 1950. In 1943 in the U.S., Heuper declared that "Asbestosis cancer of the lung is the most recent newcomer among the occupational cancers of this organ." Also Wedler, writing in German [1943a], concluded that asbestos was also a cause of malignant mesothelioma.

From the American point of view, German literature and German laws were not very popular in 1943, and the work of Nordmann and his followers received little attention. The situation was not helped by the fact that Gloyne, to whom credit for the discovery should have gone, was extremely cautious in interpreting his findings. In his 1935 report, Gloyne quoted Bridge and Henry [1928] on conditions that must be fulfilled in order that cancer be classified as industrial in origin: 1) that the incidence rate in the occupation under review should exceed that in the general population, to a significant extent; and 2) that in the occupation concerned, there should be sufficient association of the workers with a substance proved experimentally to have carcinogenic properties. These conditions are accepted by most scientists today; however, in Gloyne's lifetime, these conditions were not fulfilled with regard to asbestos and cancer. Nearly all the evidence dealt with the association of asbestosis and cancer as seen at autopsy. In a paper published posthumously in 1951, Gloyne expressed concern for the selection obviously at work in picking cases for autopsy, pointing out that necropsy records at the London Chest Hospital showed 21.3% primary lung cancer, whereas in the general population, only 2.4% of deaths from all causes at ages 15 and over were due to malignant disease of the lung.

Lynch, to whom most give credit for discovering the relationship between asbestos and lung cancer, was no less skeptical [Lynch and Cannon, 1948]. He

expressed concern not only with the problem of selection but also with the lack of experimental evidence. Only Nordmann and Sorge [1941] claimed to have produced cancer experimentally with asbestos, while experiments by Vorwald and Karr [1938], King et al. [1946], Vorwald et al. [1951], Behrens [1951], and Hueper [1955a] appeared to be negative. Moreover, Smith [1952a], in a review of animal work with asbestos, concluded that the study by Nordmann and Sorge [1941] appeared to demonstrate that asbestos did not provoke lung tumors, since of the two tumors reported in asbestos-exposed animals, one was, based on photographs presented, merely a squamous cell metaplasia, while the other, asserted to be an adenocarcinoma, "is a type of tumor that can arise spontaneously from the mouse adenoma." Even Heuper [1952] seemed to agree with this and, outside of Germany, Smith's views on Nordmann's work gained some acceptance.

Another problem in the U.S. was the attitude of leaders in the field of pneumoconiosis—particularly Vorwald [1953] and Lanza [1952]. Their expressed concern was the lack of experimental data. In addition, the possibility of a different relationship between asbestosis and lung cancer as compared with silicosis and lung cancer must have been disturbing. Lanza [1952] was also concerned about the same selectivity that worried Gloyne and Lynch, and he wondered, in regard to English claims of an association in autopsied cases of asbestosis, how many cases of lung cancer would be found if lungs from any sort of population were subject to the same minute scrutiny.

The situation could have been resolved, from the American point of view, in a report by Merewether in 1949. He compared lung or pleural cancer in cases of asbestosis reported for compensation with lung or pleural cancer in cases of silicosis, and found that 13.2% of the asbestosis cases had cancer at autopsy whereas only 1.3% of the silicosis cases had cancer. This was clearly an important study in bringing about a consensus in Great Britain. In the U.S., however, this seems to have given birth to a new idea: there is a relationship between asbestosis and cancer in England and in Germany but not in the U.S. This idea apparently originated with W.E. Smith in 1952 [1952a]; however, another Smith (K.W.) enlarged on this in 1955, stating that there was a difference due to the type of fiber used in England and Germany as compared with the U.S. In 1955, the Italian writer Rambola also felt that this was an argument for a difference between Italy and England. The argument was also repeated by Eckhardt [1959], Gilson [1960], and Johnstone and Miller [1960].

There was no answer to the question of fiber type, and it no doubt delayed acceptance by those who were uncertain as to whether a problem truly existed in the U.S. There was, however, an answer to the question concerning selection that bothered Gloyne in his 1951 article. In 1955, Doll reported on an epidemiological study of the type envisioned by Bridge and Henry [1928] in which it was shown that the incidence of lung cancer in a group of asbestos-exposed workers in England greatly exceeded that in a comparable group in the general population. This marked an end to a period when conclusions were based largely on pathological and clinical observations and opened the door for contributions by biostatisticians and epidemiologists. It probably also set back acceptance of a relationship between asbestos and cancer in the United States by another decade.

The epidemiologists demanded epidemiological evidence. In 1956, for example, Hammond and Machle stated that with regard to a relationship between asbestos and lung cancer, "there are at present too few cases and too little epidemiologic data

to establish a significant relationship.” In 1958, the Committee on Occupational Cancer of the AMA Council on Industrial Health concluded that individual case reports contribute little to an understanding of occupational cancers and that “specific increases in age, sex, and site-specific cancer incidence above normal incidences for the same age, sex, and site represent the only reliable evidence for the existence of an occupational cancer hazard.”

The first two epidemiological studies of this kind on asbestos and lung cancer in North America [Braun and Truan, 1958; Dunn et al., 1960] were considered to be negative. Thus, as late as 1961 [Johnstone] it could be stated in the “Questions and Answers” section of the *Journal of the American Medical Association* that “there is no epidemiological evidence [of an association between asbestos and lung cancer] among American workers.” Despite all of the case reports, and despite the positive epidemiologic studies by Merewether [1949] and Doll [1955], the epidemiologic evidence now seemed to be negative.

The turning point came in 1963 with the publication by Mancuso and Coulter of a positive epidemiologic study of workers from an asbestos textile plant and a study in 1964 by Selikoff et al. of asbestos insulation workers. These were followed by a 1964 conference held by the New York Academy of Sciences on the Biological Effects of Asbestos [Annals of the New York Academy of Sciences, 1965]. One session was devoted to experimental studies of asbestos and neoplasia, one to epidemiological studies of asbestos and neoplasia, and one to diffuse mesothelial tumors. Of a total of 65 papers presented, 23 dealt in varying ways with asbestos and cancer (these papers are not separately referenced here). On the question of whether asbestos caused cancer, no opinion was expressed in three papers, while 20 supported a relationship. On the question of whether asbestos caused mesothelial tumors, no opinion was expressed in four, while the remaining 19 supported a relationship. There was a considerable difference of opinion on the question as to whether it was necessary for pathologically detectable asbestosis to be present for a causal relationship between asbestos and lung cancer. As J.C. Wagner [1965] put it:

On current evidence, the earlier view that carcinoma of the lung occurs in cases with a significant degree of asbestosis is strongly supported, but information is still required to confirm that there is no correlation between exposures *per se* and these tumors (i.e. in the absence of asbestosis).

J.C. Gilson [1965], in a discussion of unresolved problems associated with human exposures to asbestos, also reflected this view. In addition, he saw as unresolved problems: 1) the relationship of the type of asbestos to asbestosis, bronchial carcinoma, and mesothelial tumors; and 2) the need for systematic prospective (epidemiological) studies of workers exposed to asbestos.

There can be no doubt that the question of whether asbestos causes carcinoma of the lung and diffuse mesothelioma of the pleura and peritoneum was settled at the 1964 conference. Probably the best indication of the views expressed at the conference and of the questions that remained to be answered is contained in the report of a Working Group on Asbestos and Cancer sponsored by the International Union Against Cancer. This working group met at the time of the conference, under the chairmanship of Thomas Mancuso, and their report was published in 1965.

In 1964, the Johns-Manville Corporation placed the following warning label on packages containing its asbestos products:

This product contains asbestos fiber. Inhalation of asbestos in excessive quantities over long periods of time may be harmful. If dust is created when this product is handled, avoid breathing the dust. If adequate ventilation control is not possible, wear respirators approved by the U.S. Bureau of Mines for pneumoconiosis-producing dusts.

CONCLUSIONS

The answer to the question as to why it took so long to accept the causal relationship between asbestos and cancer is not a simple one. Clearly, the matter involved a decision as to what is acceptable and conclusive evidence. Perhaps a special set of rules is needed for relationships like asbestos and lung cancer where some other biologic response, such as asbestosis, can be used as evidence of significant exposure, and the rules proposed by Bridge and Henry [1928] were not appropriate after all. Many writers were convinced of a relationship long before epidemiological and experimental evidence was available. Aside from the high incidence of lung cancer in asbestotics, they were impressed by the predominance of cancer in the lower lobes, the time lapse between exposure and disease, the high incidence in females, and the young age of many of the cases seen. Moreover, there were reasonable theories regarding mechanisms by which asbestos could cause cancer. These arguments were seldom acknowledged by contemporary epidemiologists and biostatisticians.

On the other hand, there were scientific reasons for delay in accepting a relationship. There were no good experimental data showing that asbestos was a carcinogen and very few positive epidemiologic data. There were political reasons, mostly reflecting the war with Germany and a rejection or lack of knowledge of much of the German scientific literature and thought during and immediately following World War II. There were economic reasons, since the asbestos industry probably exercised some control over research, and findings unfavorable to the use of asbestos were clearly not in their interest. There were cultural reasons, in that, somehow being an American during the 1940s and 1950s was being different, and ideas which originated outside of America were not readily accepted. Finally, there was a failure by the scientists themselves. Some were too modest, did not read the literature, were married to outdated ideas, or were unable to evaluate the data available to them.

Some of the problems that confronted health scientists in the past, and which delayed acceptance of a relationship between asbestos and cancer, have greatly diminished. Techniques needed for the conduct of experimental and epidemiologic studies have greatly improved; research information is much more widely available; where occupational hazards are concerned, industry is much more open with information than in the past; international political tensions have changed; more funding sources are available to conduct research; and there is better recognition that many types of cancer can be prevented and, thus, that more research is needed. On the other hand, the nature of science has probably not changed very much. Case reports, which signaled a problem with asbestos, are still given little weight; being consistent is still more important than being right; research conducted in the West is more important

than research conducted elsewhere in the world; and textbooks, upon which medical education is based, almost of necessity lag behind new knowledge. Nevertheless, health effects like those resulting from asbestos are not likely to be missed for long in the future.

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