

SEMANTICS OF THE PLACEBO*

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Whenever many different remedies are proposed for a disease, it usually means that we know very little about treating the disease, which is also true of a (remedy) when it is vaunted as a panacea or cure-all for many diseases."—Garrison

INTRODUCTION

In recent years, concurrent with increased interest in clinical methodology and the placebo effect, definitions of the placebo have proliferated. But there is little consensus among lexicographers, historians, clinicians, and researchers about how to define this word. Unknown or misunderstood semantic factors are responsible for some of the diversity of opinion.

This paper will attempt to clarify the semantics and etymology of the word, *placebo*; correct important historic errors; review the changes in definition that have appeared in medical, non-medical, psychologic, and psychiatric dictionaries; survey concepts about and definitions of the placebo that have appeared in papers on the placebo effect; and discuss the semantic, historic, and psychological factors that led to the introduction of the definition in the 18th century, and to the changes in definition since that time. Previous definitions will be critically evaluated, and the logical foundations for an adequate definition will be examined. Finally, a definition will be presented that has historic support and heuristic value.

EARLY DEFINITIONS

Before proceeding, it is important to correct several errors that have influenced histories and definitions of the placebo.

A New English Dictionary on Historical Principles (1933) is the principal reference in the English language for the origin and development of words. Its history of the placebo has two errors. The first definition of placebo was attributed erroneously to Hooper's *Quincy's Lexicon-Medicum* (1811): "Placebo... an epithet given to any medicine adopted more to please than to benefit the patient." This definition actually appeared eight years

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earlier in Fox's (1803) *A New Medical Dictionary* published in London. More serious is the omission of another definition that appeared 26 years earlier. This omission has contributed to some of the subsequent confusion about the definition.

The *New English Dictionary* (1933) was the only reference source for the history of the placebo until 1945 when Pepper (1945, 1949) published his now classic paper on the placebo.¹ Pepper corrected an important error in the *New English Dictionary*. He noted an earlier definition that appeared in the tenth edition of *Quincy's Lexicon Physico Medicum* (1787). A minor error was Pepper's failure to note that this definition actually appeared two years earlier, in the second edition of Motherby's (1785) *New Medical Dictionary*. But more importantly, Pepper, and those who followed, misquoted this definition as "a commonplace method of (sic) medicine." The actual definition, in Quincy, Motherby, and others, was "a commonplace method or medicine."

The distinction between "of" and "or" is important. The former limits the definition to medicine, whereas the latter includes any method or medicine.

CONTEMPORARY MEDICAL DICTIONARIES

Most contemporary medical dictionaries limit the definition of placebo to inert or inactive substances. These limited definitions have influenced the thinking of many physicians and nonphysicians. They conceive of the placebo only in terms of its inert qualities. If a substance has any biochemical activity whatsoever, even if given for its suggestive or psychological effect, it is often not thought of as a placebo by definition. For example, the chief of psychiatry in a major university medical school denied that placebos were used in his department. Nicotinic acid, however, was sanctioned as a nonspecific treatment but was not considered to be a placebo. His rationale was that contemporary medical dictionaries defined the placebo as inert medication. This is incorrect historically because the placebo was not limited to inert substances in major dictionaries until the middle of the twentieth century (Blakiston, 1949; Dorland, 1951; Webster, 1961).

¹Almost 25 years ago O. H. Perry Pepper published his eloquent *A Note of the Placebo*. It was one of the earliest papers devoted exclusively to the placebo effect, and the first to include the word *placebo* in the title. The paper marked the beginning of recent interest in the placebo effect. It also helped stimulate subsequent interest. The paper is a gem of medical reporting and is probably the most cited paper in placebo literature.

Before examining this in greater detail let us review the etymology more carefully.

ETYMOLOGY

The history of the placebo begins with the Hebrew Bible. Psalm 116:9 begins with the word *Ethalekh* which is the first-person singular, future indicative active of the Latin verb *placere* and means "to please, give pleasure, be approved, be pleasing, be agreeable, acceptable, to suit, satisfy." It was also used in the sense of winning the applause of an audience (Lewis, 1953). The entire sentence, *Placebo Domino in regione vivorum*, is translated as "I will please the Lord in the land of the living," or (in the King James version) "I will walk before the Lord in the land of the living." The placebo took on other liturgical meanings when it became associated with a popular Catholic rite used in the past. It was the initial word of the first antiphon and became the name commonly given to Vespers in the Office for the Dead, or Vespers for the Dead, a custom no longer used and whose meaning has become obscure (The Catholic Encyclopedia, 1911). With this usage the word entered the English language in the thirteenth century.²

The placebo took on a secular meaning in the fourteenth century and its connotation became progressively more derisive during the next several centuries: "to sing (a), play (with), make, be at the school of placebo, etc.: to play the sycophant, flatterer, be servile or time serving, Obs." (A New English Dictionary, 1933.³)

²This usage is illustrated in the following quotations from the Oxford *A New English Dictionary* (1933):

a 1225 *Aner. R.* Efter euesong anonriht siggeó ower Placebo.

c 1380 Wycliff WKS Prelatis ben more bounden to his prechyng...ban to seie matynes, masse, euen song or placebo.

c 1440 Facob's *Well.* Clerkys seydin Placebo and dirige for his soule.

1535 *Lanc. Willis.* Schall synge and say placebo and dirige on nyght.

1874 *Green Short His.* He...earned a miserable livelihood...by placebos and dirges.

³The Oxford dictionary illustrates this usage in the following quotations:

1340 *Ayenb.* Pe uerbe zenne is bet huanne hi alle zingeb 'Placebo,' bet is to zigge: 'mi ihord zayp zob me ihord dab wel.'

1386 Chaucer *Pars. T.* Flaterers been the deueles chapelleyens that syngen euere Placebo.

1483 Coxton, G. *de la Tour.* He ought...not flaterer hym ne make the placebo.

1554 Knox *Godly Lit.* Nowe they haue bene at the skool of Placebo and there they haue lerned...to daunse as the deuill hyst to pype.

1583 *Ley. Bp. St. Androis.* Plainy placebo into prices faces.

This usage derives from depreciation of the professional mourners who were paid to "sing placebos" at the bier of the deceased in substitution of the family whose role it was originally. The professional mourners probably were derogated because of their low social status, deriving income from the dead, and because they were a convenient object upon which the living could project their guilt.

A third use of the word has even more contemptible connotations: "a flatterer, sycophant, parasite" (*A New English Dictionary*, 1933) and "one who servilely echos another a toady" (Webster, 1933b). Chaucer used placebo as the proper name for a character of this sort. This usage of the word appears in various phrases between 1388 and 1572.⁴ In this etymological setting the placebo as used in medicine was born. Introduction of the word *placebo* to describe a class of treatments not previously specified was an important development in the history of methodology and medicine.

MEDICAL DICTIONARIES

As mentioned previously, the first recorded definition appeared in 1785: "a commonplace method or medicine." No earlier definitions were found in English,⁵ French, German, Italian, and Portuguese dictionaries.⁶

1607-8 Bacon *Gen. Naturalis*. If any man shall think that I have sung a placebo for mine own particular I would have him know that I am not so unseen in the world.

1679 J. P. Lett. *Friend in Country*. Where every one would sing a Placebo to the rising sun (the next Heir to the Crown).

^{4c} 1388 Chaucer *Merch*. Placebo seyede o Januarie brother (etc.). 1426 LYDG. *De Guil Pilgr*. Ffletergny... Somme callen, hir Placebo, ffer sehe kan maken an Echo Answere euere ageyn the same.

a 1572 Knox *Hist. Ref. Wks*. The Bischop... having his Placebos and Jackmen in the toun, buffatted the Frier, and called him Heretick.

a 1651 Calderwood *Hist. Kirk*. Placeboes and flatters went to court.

⁵Stephen Blankaart, chiefly relying on Gorraeus' *Definitions Medical* published in 1564 and later in 1622, published his first medical dictionary in Latin in 1679 (Blankaart, 1679) and the first medical dictionary in the English language in 1684 (Blankaart, 1684). The placebo was not defined in any of the previously mentioned dictionaries or in Blankaart's Latin-Greek dictionaries published between 1679 and 1748 (1748), Latin dictionaries published between 1717 and 1777 (1777), Greek-Latin-German dictionaries published between 1705 and 1718 (1718), the German dictionary of 1788 (1788), or in any of the Blankaart English-language dictionaries published between 1684 and 1726 (1684, 1693, 1697, 1702, 1708, 1715, 1726). No definitions appeared in the historically important Quincy dictionaries from the first edition published in 1719, to the ninth edition published in 1775 (1719, 1722, 1726, 1730, 1736,

It is not known how commonly the placebo was used in medical parlance prior to 1785. Nor do we know whether common use of the word led to the definition, or whether Motherby, fortuitously and by happenstance, but creatively, defined an uncommon use of the word which then became commonly used in medicine. Although it is possible that common use of the word led to the definition, as we shall see later, definitions appearing in dictionaries by happenstance can often lead to common use.⁷ The explanation is partially supported by the sudden appearance of the definition. References are not found in medical literature prior to 1785, and are infrequent after 1785. Confirmation will require further historical research.⁸

1743, 1757, 1767, 1775), in the improved James dictionary (1745), and in the first edition of Motherby's dictionary (1775).

⁶A survey of major dictionaries published in France, Germany, Italy, and Portugal revealed no earlier definitions. Definitions begin to appear in these languages many years after their appearance in the English language. So it is likely that the definition of the placebo originated in England. This is not surprising because England was increasingly the center of medical knowledge from the sixteenth to the eighteenth centuries. (See also discussion.)

⁷See Murray's (1900) description of the changes in the English language caused by Samuel Johnson's misspelling of dispatch and reversal of coco and cacao.

⁸The placebo surprisingly was not defined in many dictionaries published during the 19th and 20th centuries: Hooper (1798-1809), Turton (1802), Macaulay (1828-1858), Copland (1837-1860), the London Hoblyn (1835), the 2-volume Quain dictionary (1883-1903), Dorland (1900-1953), Barton & Wells (1903), Gould (1904-1915), Paley and Halpern (1937) and in the first seventeen editions of *Black's Medical Dictionary* (1906-1942). See also references in psychiatric dictionary history.

The word placebo was cited infrequently in medical literature prior to the 20th century. Only two references are cited by *A New English Dictionary* (1933):

1824 Scott St. Rouan's—There is nothing serious intended—a mere placebo—just a divertissement to cheer the spirits and assist the waters;

1885-1888 Fagge & Pye-Smith, *Princ. Med.*—It is probably a mere placebo, but there is every reason to please as well as cure our patients.

G. Stanley Hall (1887) refers to the placebo in a review of telepathy: "Physicians appeal to the imagination in desperate cases with bread pills and placebos."

Many papers, although discussing phenomena which today would be referred to as placebos or placebo effects do not mention the word *placebo*: See Parr's (1809) discussion of quackery, Reid's (1823) *Essays on Hypochondriasis, and Other Nervous Affections*, Mackay's (1841) discussion of *Alchemists and Magnetizer's*, Holmes' (1891) discussion of *Homeopathy and its Kindred Delusions* in 1842, Osler's (1905) *Medicine in the Nineteenth Century*, and the American Medical Association's *Nostrums and Quackery* (1921). Also see Twain (1899), Parker (1908, 1909a, 1909b), Glover (1931), Schmideberg (1838, 1958), Weitzenhoffer (1953), Young (1961), and the summaries in Shapiro (1960a) of Rivers, Bernheim, Janet, Freud, Ferenczi, Jones, Hollingsworth, and Glover.

Even in the 20th century, the *placebo* has become a popular and commonly used word only in the last ten years (Shapiro, 1960a).

Although the precise origin of the placebo is uncertain, quasi-official recognition occurred when it was defined in the latter half of the 18th century. Now some treatments had an official name by which they could be described. The original definition, "a commonplace method or medicine," subsequently appeared in Quincy (1787, 1794, 1802), *American Medical Lexicon* (1811), Motherby (1795, 1801), and Parr (1809, 1819, 1820a, 1820b).

Contempt and derogation characterized the premedical etymology of the placebo, and is reflected in the use of "commonplace" in the original medical definition. "Commonplace" refers to that which is common, trite and pedestrian (Webster, 1838), or "a cliché, superficial, used often, without originality or freshness, ordinary, dull, trite and stale" (Webster, 1961). The derisive intent was reflected in the first change in definition which appeared in Motherby (1795, 1801), and later in Parr (1809, 1820a, 1820b): "a commonplace method or medicine calculated to amuse for a time, rather than for any other purpose."

This connotation also characterized the next change in definition: "I will please, an epithet given to any medicine adapted more to please than benefit the patient." It first appeared in Fox (1803), and was repeated in Coxe (1808, 1817), in eight editions of the London Hooper (1811, 1820, 1825, 1839, 1848), and in thirteen editions of the American Hooper (1817, 1822, 1824, 1826, 1829, 1838, 1841). This definition with minor variations became the traditional one in America and England during the 19th century and the first half of 20th century.⁹

⁹The history of the definition in American medical dictionaries may be of interest:

The placebo was defined as "a commonplace method or medicine" in the first American medical dictionary published by Swords (Quincy, 1802). The same definition appeared in a subsequent edition (*American Medical Lexicon*, 1811). The second American medical dictionary was the *Philadelphia Medical Dictionary* (Coxe, 1808, 1817); the placebo was defined: "I will please; an epithet given to any medicine adapted more to please than benefit the patient." In 1820 the London 1809 Parr (1820a, 1820b) was published in America; the definition was the same as in Motherby ("a commonplace method or medicine calculated to amuse for a time, rather than for any other purpose").

Variations in the definitions appear as "I will please, an epithet given to any medicine, intended rather to satisfy the patient than cure a disease" (Dunglison, 1833-1846), "a medicine prescribed rather to satisfy the patient than with any expectation of its effecting a cure" (Dunglison, 1854-1903), and "I will please"; a term for medicine given rather to please than to benefit a patient (Edinburgh, 1836).

An interesting variation in definition appeared in the last edition of Hooper (1848): "An epithet given to any medicine administered rather to amuse the mind of the patient than to fulfill any definite therapeutic intention. It must not be supposed

The first allusion to the placebo as an inert substance occurred at the end of the last century. Foster's (1894) dictionary, with attribution to a Reverend George M'Arthur, defined the placebo as "a make-believe medicine, sometimes administered for its effect on the patient's imagination rather than because it is of medicinal value." The reasons are not known for the use of the term *make-believe*. Foster's dictionary was later published as *Appleton's Medical Dictionary* (1904-1915). This definition, surprisingly, reappeared in an important and commonly used medical dictionary 55 years later (Dorland, 1947) and may have contributed to the change in definition which occurred recently.

Prior to 1947 the Dorland (1900-1944) *American Illustrated Medical Dictionary* had defined the placebo traditionally as "a medicine given to please and gratify the patient." Inexplicably, the inadequate Foster (1894) definition reappeared in the 21st edition (Dorland, 1947): "a make-believe medicine given to please or gratify the patient." The reason for the change is not known by the editor of Dorland dictionaries because source files were not kept, and the editor responsible for that edition has died (Husted, 1963). The definition may have contributed to Dorland's decision to define the placebo in a totally different way in its next edition (Dorland, 1951): "an inactive substance or preparation formerly given to please or gratify a patient, now also used

that such administrations are useless; the sensorium often exercises great influence on disease." This addendum to the definition probably reflected growing awareness of the psychological effects of placebos, but it failed to influence definitions that appeared subsequently: "Literally, though incorrectly, I will please, a term applied to any medicine given to please or humor the patient, as a gold pill, e.c." (Hoblyn, London 1858-1909, American 1845-1900), "a medicine to amuse rather than benefit" (Cleveland, 1855-1888); "a term for a medicine given rather to please than with any purpose or hope of benefiting a patient" (Mayne, 1860); "applied to a medicine given rather to please than benefit a patient" (Mayne, 1868); "I will please or sooth, applied to a medicine given rather to please than benefit the patient" (Thomas, 1864-1874); "anything prescribed for the purpose of pleasing or humoring the whim of a patient rather than for its therapeutic effect" (Gould, 1890-1915); "a medicine exhibited to satisfy a patient" (Keating and Hamilton, 1892); "a medicine given rather to please the patient than to benefit him directly" (Lippincott, 1897-1913); "name for a medicine given by a doctor to a patient simply to please or satisfy the patient's mind; usually of a harmless nature; e.g., water colored with cochineal (New Sydenham 1899); "a medicine given to please or gratify the patient" (Dorland, 1900-1944); "a medicine given simply to gratify a patient or produce an effect upon his imagination" (Duane, 1902); "a medicine given for the purpose of pleasing or humoring the patient, rather than for its therapeutic effects" (Gould, 1926-1941); "a treatment, especially a medicine given to humor the patient" (Faber, 1953; Macmillan, 1954).

in controlled studies to determine the efficacy of medicinal substances." According to the editor, a possible reason for the change was the "feeling that a make-believe medicine was not a very suitable phrase to appear in a scientific dictionary, or even properly representative of the truth" (Husted, 1963).

These events illustrate how a definition of questionable merit and source may contribute to important changes in the concept and definition of a word (see footnote 7). The first reference to the research use of placebos appeared in Dorland (1951), and reflects another change and trend in the placebo's history.

The change, however, was not due to happenstance only. Although most dictionaries continued to define the placebo in the traditional manner, this subtle change in definition occurred in other dictionaries. The first edition of the non-medical *Funk & Wagnalls* (1893) dictionary defined the placebo as "any harmless substance, as bread pills, given to sooth a patient's anxiety rather than as a remedy."¹⁰⁻¹² The New Sydenham (1899) dictionary added "usually of a harmless nature, e.g. water colored with cochineal" to the traditional definition. Reflecting and possibly contributing to the change, the definition in the first edition of the Stedman (1911) medical dictionary was "an indifferent substance in the form of a medicine, given for the moral or suggestive effect."¹³ This definition has been repeated in 19 editions of Stedman (1913-1961) dictionaries.¹⁴

¹⁰Definitions in several nonmedical dictionaries were included in this section if they were considered important in the history of the placebo.

¹¹The reference source for this definition is given as the first volume of the *American Journal of Psychology* (1887). The editor, G. Stanley Hall, in reviewing research on telepathy, mentions parenthetically and without any relevance to a discussion of the placebo, that "physicians appeal to the imagination in desperate cases with bread pills and placebos..." Although Funk & Wagnalls equates the placebo with "bread pills" by citing it as an example of a placebo, Hall makes no such definite equation. This definition has been continued in all subsequent editions of Funk & Wagnalls (1913-1961) dictionaries.

¹²This definition is interesting in other ways. Anxiety is proposed as a psychological factor in placebo reactions for the first time.

¹³Information about the original definition is not available because of the death of the original editor, Thomas Lathrop Stedman, and because source files for definitions were not kept (Cochrane, 1963).

¹⁴Reference to the research use of placebos is appended to the original definition in the 20th edition of Stedman (1961): "an inert compound, identical in appearance with material being tested in experimental research, where the patient and the physician may or may not know which is which."

The word *inactive* initially appeared in the definition of a non-medical dictionary. It was added parenthetically to the traditional definition in the second edition of *Webster's New International Dictionary* (1933b): "a medicine, or preparation, especially an inactive one, given merely to satisfy a patient." This was the first use of the word *inactive* in a definition of the placebo.¹⁵

The definition that first limited the placebo to inactive substances appeared a few years later in the abridged but popular Taber (1937) medical dictionary: "Placebo, inactive substance given to satisfy patient's demands for medicine; such as bread pills" (Taber 1937, 1938, 1940, 1951, 1963a). It is now difficult to determine whether Taber defined the placebo idiosyncratically, or whether his definition reflected a change in medical thinking about the placebo. The Taber definition probably had little influence on subsequent definitions, however, because other dictionaries did not revise their definitions until much later.¹⁶

The next citation of the placebo as inert appeared in *A Simplified Medical Dictionary for Lawyers* (Maloy, 1942). The placebo was defined as "an inert medicine given to please and satisfy a patient who thinks medicine is required."

The *Blakiston's New Gould Medical Dictionary* (1949) was the first major dictionary to limit the definition to inactive medicine. The placebo was defined as "a medicine having no pharmacologic

¹⁵According to Kay (1963) of Webster's dictionary, this definition stems from the late Dr. Esmond Long of the Henry Phipps Institute.

¹⁶The first citation of the placebo as inert may actually go back to 1905. Clarence Wilbur Taber (1963b) stated in a personal communication that his first medical dictionary was *Taber's Medical Dictionary for Nurses*. The placebo was defined as "An inert drug given to satisfy a patient." Taber added: "This dictionary was first published by myself; later by Laird and Lee of Chicago. Later incorporated in my present dictionary by F. H. Davis Co."

Taber's (1963b) rationale for the change in definition was: "A lexicographer is supposed to use his own phraseology as I have used the word 'inactive' and not to copy the definitions of other authors or compilers. The term 'inert' seemed more definitive than others used in this connection... In a small or abridged dictionary one has to conserve space and so many of my definitions consist of no more words than absolutely necessary making it possible to treat more important words at considerable length." (See footnote 7 and comments preceding the footnote.) Taber objected to many of the current definitions, stating, "A placebo is not a medicine but a substitute for one. It is not given to satisfy, please, soothe... It is really given to deceive the patient by making him think he is being given a real drug or prescription."

Taber's definition is based on ethical rather than historic or heuristic principles, and it reflects early 20th century attitudes toward the placebo. Strong ethical values about the placebo tend to limit the definition (See Shapiro 1960b).

effect, but given for the purpose of pleasing or humoring the patient."^{17, 18} This trend was continued in other dictionaries. The change in the Dorland (1951) dictionary was mentioned previously. The *Putnam Medical Dictionary* (1961) defined the placebo as "inert substance, in the form of a medicine, given for its psychic or suggestive effect." The revised definition in the *Webster's Third New International Dictionary* (1961) was "an inert medication or preparation given for its psychological effect especially to satisfy the patient or to act as a control in experimental series." According to the editor (Kay, 1963) the definition "is based on abundant citations of usage both at the professional and the popular level and we believe it accurately reflects normal current usage." Dr. Kay stressed, however, that "the pertinent meaning of *inert* in this context is 'powerless for an expected or desired biological effect' rather than the more general 'not having or manifesting active qualities.'" In other words, the term *inert* was used operationally and not meant to be taken literally. Unfortunately, this explanation is not conveyed by the definition.

Medical and nonmedical etymologies rely on erroneous historical sources and do not contribute to our understanding (Pepper, 1949; Weekley, 1952; Skinner, 1949, 1961; Wain, 1958).¹⁹

NONMEDICAL DICTIONARIES

The placebo was not defined in nonmedical English dictionaries* until the middle of the 19th century.

Webster (1828, 1838, 1844, 1845, 1846, 1847) dictionaries did not define the placebo until 1847. The first definition was "in

¹⁷Gould dictionaries had defined the placebo previously (since 1880) as "anything prescribed for the purpose of pleasing or humoring the whim of a patient rather than for its therapeutic effect" (Gould, 1890-1915) and as "a medicine given for the purpose of pleasing or humoring the patient rather than for its therapeutic effect" (Gould, 1926-1941).

¹⁸No explanation for the change in definition could be given by the editor of the *Blakiston's New Gould Medical Dictionary* (Keller 1963).

¹⁹Skinner (1949, 1961), in the *Origin of Medical Terms*, refers to the placebo as "a term applied to a medicine, which is given to please or satisfy the patient rather than for any specific benefit. It is in Hooper's Medical Dictionary for 1811." In *Medical Etymology*, Pepper (1949) quotes Quincy's Lexicon of 1787 incorrectly as "a commonplace method of (sic) medicine." In Wain's (1958) *The Story Behind the Word*, the placebo is referred to as "a prescription given by a physician to please rather than to benefit the patient." Weekley (1952) refers only to the ecclesiastical derivation: "Initial word of antiphon in Vespers for the dead, Psalm CXIV:9 (Vulgate)."

*Refs. 8-10, 50, 185-189, 197, 287, 289, 309-311, 348.

medicine, a prescription more to please than benefit the patient" (Forsythe).²⁰⁻²²

The 1933 Webster (1933a) dictionary added to the etymology of the placebo. Previously noted was Webster's (1933b) parenthetical reference to the placebo as an inactive medicine in its second edition, and the final change in *Webster's Third New International Dictionary* (1961) where the placebo was referred to as an "inert medicament or preparation."

The placebo was defined in the traditional manner of the 19th century in a number of other nonmedical dictionaries.^{*23}

The Funk & Wagnalls (1893) definition originally appeared in 1890: "any harmless substance, as bread pills, given to sooth the patient's anxiety rather than as a remedy," and has been repeated in all subsequent editions (1895, 1901, 1913-1961). Its historical relevance and shortcomings have been discussed previously.

The inaccuracies in the authoritative *New English Dictionary on Historic Principles* (1933) were mentioned previously: The original definition was attributed erroneously to Hooper (1811). This dictionary has extensive etymological references.

NON-ENGLISH LANGUAGE DICTIONARIES

A random survey of non-English language dictionaries contributes little to our understanding of the placebo's history. The French and Italian nonmedical history paralleled the English.

²⁰The attribution to "Forsythe," according to the present editors of Webster, is a source that cannot be identified (Kay, 1963).

²¹The first citation of the *placebo* as the initial word in the Roman Catholic Vesper hymn for the dead appeared in Webster and was attributed to Fosbroke (Webster, 1847).

²²As in medical dictionaries, Webster's definitions changed only slightly throughout the years: "in medicine a prescription more to please than benefit the patient" (1848-1861); "a prescription intended rather to please or satisfy than to benefit the patient" (1864-1888); "a prescription intended to humor or satisfy" (1890-1933). The Webster dictionary of 1890 first referred to Chaucer's use of the word "*Placebo*."

*Refs. 48, 49, 100, 246, 250, 312, 313, 388, 389.

²³The placebo was defined in the Ogilville (1855-1883) *Imperial Dictionary of the English Language* as "an epithet given to any medicine adapted rather to please than benefit the patient"; in the Worcester (1860, 1874) *Dictionary of the English Language* as "a medicine prescribed rather to satisfy the patient without any expectation of effecting a cure. Dunglison"; in the Hunter and Morris *Encyclopedic Dictionary* (1896) as "a medicine calculated rather to please than to benefit the patient"; in the *Century Dictionary* (1890-1911) as "a medicine adapted rather to please than to benefit a patient," with etymological contributions to the placebo's archaic use; and in the *Shorter Oxford English Dictionary* (1933-1947) as "a medicine given more to please than to benefit the patient."

The medical use of the term *placebo* occurred much later, however, in France (*Dictionnaire de la Langue Française* 1873, Larousse 1874, Godefroy 1881, *Dictionnaire Encyclopedique des Sciences Médicales* 1885, *Encyclopédie Universelle* 1908), and in Italy (Tammaseo 1861-1879, *Dizionario Enciclopedico Italiano* 1958). No references to the nonmedical use of the placebo, and only recent medical definitions, were found in German, Spanish, and Portuguese dictionaries (Brockhaus 1886, *Der Grofze Brockhaus* 1933, *Der Neue Brockhaus* 1959, Meyer's Lexicon 1928, *Dizionario Enciclopedico Hispano-Americano* 1894).

PSYCHIATRIC AND PSYCHOLOGICAL DICTIONARIES

Definitions of the placebo were not included in psychological and psychiatric dictionaries until recently. Their absence paralleled the belated interest of psychologists and psychiatrists in the placebo effect (Shapiro, 1960a, b) and might reflect defensiveness about placebo phenomena.

Definitions are not included in Tuke (1892), Baldwin (1901-1905), Warren (1934), Hutchings (1930, 1939, 1943), Kahn (1940), Stone (1944), Sadler (1945), Fodor and Gaynor (1950), Drever (1952), Kupper (1953), the important Hinsie and Shatzky (1940, 1953, 1956), and the American Psychiatric Association's *A Psychiatric Glossary* (1957).

The first definition of placebo in a psychological or psychiatric dictionary appeared in the *New Dictionary of Psychology* (Harriman, 1947). It was defined traditionally as "a pill or a liquid given to humor the patient with a psychoneurotic disorder. Its therapeutic effects, if any, are psychological, not physiological."²⁴

The English and English (1958) dictionary defined the placebo as "a preparation containing no medicine (or no medicine related to the complaint) and administered to cause the patient to believe he is receiving treatment." This definition includes active medication that is without specific activity for the complaint or operationally inactive for the condition being treated.

The most comprehensive definition appeared in the third edition of the *Psychiatric Dictionary* edited by Hinsie and Campbell

²⁴The definition in Harriman (1959) was "a harmless medication which the patient believes to be a cure for his or her ailment."

(1960).²⁵ This definition, based primarily on the ideas of John C. Whitehorn (1958), dispenses with the defensive "humoring of the patient," acknowledges the effectiveness of placebos on psychologic as well as psychophysiologic symptoms, includes active and inactive medication, and recognizes the importance of active placebos as adequate controls in research. For the first time a mechanism is proposed to explain placebo effects. They are related to the patient's expectations and other factors. The exclusion of psychological methods of treatment, however, by limiting the definition to medication, is a serious shortcoming.

A definition of the placebo was included in the second edition of *A Psychiatric Glossary* (1964),²⁶ which was published by the American Psychiatric Association seven years after the first edition. This definition is a compromise between the limited definitions of the past and the extensive definitions that have begun to appear in dictionaries and papers on the placebo effect. It includes the therapeutic and experimental use of the placebo and the concept of the negative (side effect) placebo effect, although it limits the definition to inert medicine. A more inclusive but non-specific mechanism is proposed to explain the placebo effect.

The inclusion of the definition in these dictionaries followed the increased interest of psychiatrists and other medical men in the placebo effect, double blind studies, and scientific methodology. They appeared concurrent with the increase in the number of papers on the placebo effect in the last decade (Shapiro, 1959,

²⁵(L. "I am to placate.") Any medication used to relieve symptoms, not by reason of specific pharmacologic action but solely by reinforcing the patient's favorable expectancies from treatment. Although a placebo may be an inert substance, as used in present-day research placebos more commonly contain active substances that at least in part mimic the side-effects of the specific therapeutic agent with which the placebo is being compared. Placebo effects include all those psychologic and psychophysiologic benefits and undesirable reactions which reflect the patient's expectations; they depend upon the diminution or augmentation of apprehension produced by the symbolism of medication or by the symbolic implications of the physician's behavior and attitudes."

²⁶"Placebo: Originally, an inactive substance given to 'placate' a patient who demands medication (e.g., "a bread pill"). In modern usage, a pharmacologically inert substance administered for therapeutic or experimental reasons because of its potential psychological effect. May be therapeutic or noxious in its effect due to suggestion by the therapist or experimenter or due to the patient's self-induced expectations (faith, fear, apprehension, hostility, etc.). In British usage a placebo is sometimes called a 'dummy.'"

1960a).²⁷ Although definitions in psychiatric dictionaries are more advanced than those in nonpsychiatric dictionaries, the most extensive, operational, and advanced definitions appear in papers on the placebo effect.

PAPERS ON THE PLACEBO

In a survey of the literature, 69 papers were found that discussed the definition, concept, or use of the term *placebo*. Most of the papers proposed expanded definitions. These differed from the limited and classical definitions that have appeared in most dictionaries.²⁸

Many authors* agreed with the editorial comment in the *Journal of the American Medical Association* (1955) that "most dictionary definitions of the placebo are too restrictive for modern usage."

Definitions of placebo were limited to inert or inactive substances or medication in twelve papers.**

Twenty-six papers*** by nonpsychiatrists included active medication in their definitions.

Thirty-one psychiatric papers† included active medication in their definitions.

While eight papers‡ limited their definitions to knowing or deliberate use of placebos or nonspecific active medication, 23 papers†† included the unknowing use of placebos. This included

²⁷Interest in placebo phenomena has continued to increase; more papers have probably been written on the placebo effect in the last three years than in all previous years combined.

²⁸References cited in this section include papers which propose definitions and discuss concepts or usage of both the placebo and placebo effect. Although the placebo and placebo effect can be defined differently (e.g., the placebo is defined as inert, and the placebo effect as the effect of nonspecific treatment), because of the looseness and interchangeable use of these terms in the literature, no differentiation has been made in the cited references. For example, note how the placebo is defined by reference to the placebo effect in Taber (1957), Wolf (1959a, b) and Shapiro (1959, 1960a), and the interchangeable use of placebo effect, placebo response, and placebo reaction. Definitions which have appeared in the literature are quoted in footnote 29.

*Refs. 52, 58, 113, 132, 153-155, 176, 213, 237, 291, 297-299, 302, 304, 380, 385, 386, 391.

**Refs. 13, 42, 112-114, 135, 210, 212, 261, 345, 349, 391.

***Refs. 1, 43, 52, 59, 82, 104, 105, 107, 115, 132, 176, 181, 191, 193, 207, 213, 217, 237, 238, 291, 292, 317, 385, 386, 387, 392.

†Refs. 2, 44, 58, 108, 111, 130, 134, 153-155, 157, 200-202, 205, 206, 214, 215, 218, 223, 229, 284, 297-299, 302, 304, 307, 308, 380, 382, 383, 393.

‡Refs. 59, 104, 105, 153-155, 213, 380.

††Refs. 44, 52, 82, 107, 108, 115, 154, 155, 157, 176, 181, 191, 202, 215, 237, 238, 292, 297, 298, 299, 302, 385, 386, 393.

therapy of all sorts which the physician prescribed in the belief that it was effective or specific, even though objectively and unknown to the physician, the therapy or procedure had been demonstrated in the past, or would be shown in the future, to be ineffective or nonspecific.

Therapies that were believed effective or specific in the past but which were later demonstrated to be ineffective or nonspecific were referred to as placebos in 20 papers.*

Treatment methods other than medication, such as heat, inhalants, various preparations, mechanical procedures, surgery, and so forth, were included in the definitions of 22 papers.**

The use of placebos in research is a recent addition to the definition and has appeared in more than 25 dictionaries and papers.***

Psychotherapy is the most recent addition to the definition, and is referred to in 21 papers.†

In summary, the literature on the placebo and placebo effect proposes an expanded definition, concept, or use of the term *placebo*. These differ considerably from those proposed in most medical and nonmedical dictionaries.

Examples of definitions and ideas about the placebo which have appeared in medical literature are listed below:

Gold (1946): "...a placebo is...a chemical device for psychotherapy..."

Clyne (1953): "A placebo is any treatment that is not fully understood in its implications."

Gaddum (1954): "A placebo is something which is intended to act through a psychological mechanism."

Leslie (1954): "A placebo is a medicine or preparation which has no inherent pertinent pharmacologic activity but which is effective only by virtue of the factor of suggestion attendant upon its administration. The substance may be injected, inserted, inhaled or applied."

DeMaar and Pelikan (1955): "The placebo may still be considered, as it was in the time of Hooper, as one of those chemical substances with negligible intrinsic pharmacologic potency."

*Refs. 13, 44, 59, 107, 113, 130, 157, 158, 176, 202, 213, 214, 218, 237, 292, 297-299, 302, 385, 386.

**Refs. 2, 15, 44, 52, 108, 131, 134, 157, 158, 200, 213-215, 218, 223, 235, 237, 292, 297-299, 302, 393.

***Refs. 43, 58, 78, 113, 153-155, 191, 204, 205, 207, 213, 223, 235, 284, 291, 292, 298, 302, 315, 335, 345, 349, 383, 385, 386.

†Refs. 108, 157, 153, 200, 202, 214, 215, 218, 237, 286, 299-292, 297, 299, 302, 394, 305, 349, 386, 393.

This paper illustrates how easy it is to misquote. The first definition is quoted as "a commonplace in (sic) medicine," which is a misquote of Pepper's (1945) quotation, "a commonplace method of (sic) medicine," which is a misquote of Motherby's (1785) definition, "a commonplace method or medicine." See also Rubinstein (1961): "a commonplace medicine."

Lasagna (1955): "Placebo is a word '... to describe an inactive, harmless pill or injection which is given solely for its psychological effect on the patient.'"

Snell (1956): "a definition... for the term 'placebo'... non-specific stimulus."

Fisher and Dlin (1956): "A placebo may be any object offered with therapeutic intent... The 'placebo reaction' occurs in psychotherapy..."

Rosenthal and Frank (1956): "... the placebo effect... may be thought of as nonspecific form of psychotherapy and it may produce end-organ changes and relief from distress of considerable duration... To show that a specific form of psychotherapy based on a theory of personality and neurosis produces results not attributable to the non-specific placebo effect it is not sufficient to compare its result with changes in patients receiving no treatment. The only adequate control would be another form of therapy in which patients had equal faith, so that the placebo effect operated equally in both, but which would not be expected by the theory of therapy being studied to produce the same effects."

Modell and Houde (1958): "As the word is presently used in clinical evaluations, it includes a large series of visceral, somatic, and psychic responses resulting from the symbolic implications of the physician, his ministrations and his medicaments."

Hollander (1958a, b): "A placebo is a pharmacologically inactive substance for the patient *for whom* it is prescribed... The physician who prescribes it is *aware* of the fact. Knowing this he prescribes the substance for its psychotherapeutic effect... The physician may *deny* that an inactive preparation is inactive. One can deny only what one knows at some level... and therefore the doctor does know."

Imber et al. (1957): "... the placebo effect was defined as those changes in the patient produced primarily 'by the patient's faith in the efficacy of the therapist and his technique.' (Rosenthal and Frank 1956)"

Rashkis and Smarr (1957): "Placebo is a medication ordered by the doctor having the same apparent physical characteristics as the active agent, given by the same root of administration, yet not having the same specific therapeutic action."

Whitehorn (1958): "A medication which is used to relieve a patient's distress, without specific pharmacologic action, solely by its power to reinforce his favorable expectancies, has become known as a placebo..."

every medication, or other therapeutic procedure, may have both inherent potency and placebo potency. This generalization would include psychotherapy."

Wolf (1959a): "...placebos... a new definition. A placebo effect is that which is attributable to the administration of an agent but not to its pharmacodynamic properties."

Wolf (1959b): "...placebos... a new definition... Placebo effect, any effect attributable to a pill, potion, as procedure, but not to its pharmacodynamic or specific properties."

Greenblatt et al. (1959): "...placebo, i.e., when it (the drug) has no specific, disease-combating efficacy."

Shapiro (1959, 1960a): "...placebo effect... the psychological physiological or psychophysiological effect of any medication or procedure given with therapeutic intent, which is independent of or minimally related to the pharmacologic effects of the medication or to the specific effects of the procedure, and which operates through a psychological mechanism."

Shapiro (1960b, 1963, 1964b, c): Definitions in these papers are incorporated in the definition proposed at the end of this paper and need not be repeated here.

Knowlis and Lucas (1960): "The placebo response may well be an important component of many established treatments both physical and psychological..."

Spectrum (1960): The trend toward extensive definition of the placebo is further reflected in a recent paper in a journal distributed to physicians by pharmaceutical manufacturers: "...the placebo in its broad definition... is... a substance administered, or a procedure undertaken, without any possibility of specific action..." Previously such drug journals had limited the definition to the more limited inert drug (Physician's Bulletin 1955a, b; Spectrum 1957; Hospital Focus 1964).

Roueché (1961): This sophisticated article by the well-known science writer, Berton Roueché, appearing in *The New Yorker*, reflects the growing significance and importance of the placebo and of placebo effects. Roueché states that, "The definition of a placebo has broadened... it now embraces any form of therapy that is appropriate to the complaint under treatment. All medical procedures may thus on occasion be placebos (So, for that matter, may also anything...) ... A true drug becomes a placebo when its specific therapeutic properties are misapplied."

Rubinstein (1961): "A placebo refers to a substance, procedure or other intervention that is presumed to be neutral in regard to a given outcome, while an agent may be referred to as a drug, procedure, or other intervention designed to *bring about* a given outcome. We may, however, anticipate that no definite implications can be made that the placebo itself or the agent itself is in fact the cause that brings about the results

of treatment. . . The placebo reaction may be produced with equal facility by quacks, charlatans and honest physicians. Formal rituals, religious symbols, mechanical, surgical and physical agents, as well as psychotherapeutic techniques may produce placebo reactions which cannot be attributed alone to the intrinsic properties of the technique employed."

Lesse (1962): After quoting Shapiro's (1959) definition, Lesse adds, "This may be further expanded to include the observations that the relative or complete remission or exacerbation of any symptom, sign or syndrome as the result of the administration of any drug or technique, cannot be ascribed to the specific effect of the drug or technique on the symptom, sign or syndrome unless it first can be demonstrated that the improvement or worsening is not due to a non-specific or placebo effect. . . Placebo reactions play an intimate part in *all* psychotherapeutic procedures.

See Lesse (1964) for an attempt to classify placebos.

Liberman (1962): "Any medical procedure that produces an effect in a patient because of its therapeutic intent and not its specific nature (chemical or physical) is called a placebo."

Honigfeld (1963): "The 'placebo effect' refers to any effect of medical intervention which cannot be attributed to the specific action of the drug or treatment given."

Braceland (1963): "Placebo usually refers to a substance administered by the doctor whose aim it is to help the patient and thereby please himself. A placebo is devoid of psychopharmacodynamic properties; it can be an inert pill or an innocuous injection which should logically have no effect on symptoms arising from disturbed physiology or an ailing organ. Yet it often does."

DISCUSSION

Origin of the Medical Definition

The reasons for the introduction of the word *placebo* into medicine in 1785 are largely unknown. But major contributing factors are scientific progress in medicine and the defensiveness of physicians.

Medical advances during the 17th and 18th centuries can be summarized as follows: the overthrow of Galenical medicine (Garrison, 1921; Bull, 1959); the introduction of several important specific drugs in treatment, such as cinchona bark, foxglove, limes for scurvy, and inoculation for smallpox (Garrison, 1921); reforms in the pharmacopoeias (Garrison, 1921; Bull 1959); increased use of controlled clinical trials (Bull, 1959); the remarkable successes of quackery (Garrison, 1921; Walker, 1959); the general development of medicine (Garrison, 1921) and the in-

creased intellectual and professional security of physicians (Garrison, 1921).

Defensive factors might have contributed to the first definition (Shapiro, 1960a, b). Despite medical advances, the vast majority of treatments were ineffective or placebos (Shapiro, 1959, 1960a). Secret remedies characterized the treatment of both quack and physician (Garrison, 1921). It was not easy to differentiate quack and physician on almost any criteria (Walker, 1959). Physicians occasionally rejected important contributions by quacks who often received official recognition by reigning royalty (Suran-Reynals, 1946; Walker, 1959). It was a period of heated disputation; physicians vehemently railed against quacks and other physicians (Garrison, 1921; King, 1958; Shapiro, 1960a). If the term *placebo* arose, in part, as a way for the physician to depreciate the treatment of the quack, the derogation rebounds on the physician because their treatment was probably not much better and at times actually more harmful (King, 1958). Physicians may have become sensitive to the inadequacy of their ministrations. The derisive character of the epithet *placebo* suggests that it was a defensive appellation applied to the treatments used by others, much as today physicians attribute this practice not to themselves but to other physicians (Hofling, 1955; Shapiro, 1960b). Attributing the patient with being amused, pleased, or humored by a placebo suggests a projective mechanism in which the physician disowns feelings of impotence, hostility, or guilt by attributing patients with foolishly requesting and responding to placebos (Parsons, 1951; Clyne, 1953; Hofling, 1955; DeMaar and Pelikan, 1955; Whitehorn, 1958; Frank, 1958; Shapiro, 1959, 1960a, b, 1963).

Although the original definition defined the placebo as a treatment knowingly prescribed for its psychological effect, it is likely that the knowing use of placebos was infrequent. It is probable that physicians denied their use of placebos and attributed this practice to derogated colleagues.

The *placebo* was a pejorative and not a scientific term. This may explain why it was used so infrequently in the past. Although the placebo is a common word in medicine today, it was hardly used during the first hundred years of its existence. The author has not been able to find any reference to its use in medicine, other than in dictionaries, until 1887. Although as early as the 19th century many papers discussed what we would refer to

now as the placebo effect,²⁹ the word *placebo* was infrequently used, and the term *placebo* effect has been used only within the last 15 years.³⁰

Treatments Included in the Original Definition

There was no implication in the original definition, or in those that followed for a hundred years, that the placebo was limited to, or even included, inert or inactive substances. In fact, it is doubtful that there was any significant conscious prescribing of inert medication such as sugar pills. Such substances do not appear in the formularies or pharmacopoeias of the period. It is probable that if placebos were knowingly used they were chosen from a group of drugs believed to be active but not very active. The judgment that the medications used in the past were placebos is that of hindsight and not the evaluation of the physicians who used the medication (Pepper, 1945; DeMaar and Pelikan, 1955; Shapiro, 1959, 1960).

The inclusion of treatment other than medication in the original definition may have derived from the 18th century use of methods such as Franklinism, Galvinism, Mesmerism, celestial beds, laying on the hands, Perkins' tractors, and so forth.

Definition Limited to Medicine

Definitions of the placebo were increasingly limited to medicines during the 19th century. Methods disappeared entirely although vague entities like "treatment" and "anything" did continue in some definitions. The probable reason for this change was that nondrug treatment declined in importance during the first half of the 19th century, and medical practice became characterized by drug treatment. This was reflected in the treatments used by quacks, who usually follow and exploit those areas legitimately developed by scientific medicine (Garrison, 1921; Walker, 1959). The 19th century has been described as the great age of the patented, secret preparation, or nostrum, and the predominant quack activity during that period was the use of these

²⁹See references in footnote 8 and definition in the last edition of *Hooper Quincy Lexicon-Medicum* (1848).

³⁰The term *placebo effect* appears in medical literature concurrent with the use of the term *double blind* and the widespread introduction of controlled methodology in the evaluation of treatment during the past 15 years.

drugs (Garrison, 1921; Young, 1961). As a parallel development, placebo definitions gradually became limited to medicine.

Another factor was the 19th century interest in hypnotism and suggestion. At that time suggestion included many psychological and treatment phenomena which today are referred to as placebo effects (Bernheim, 1839; Janet, 1924, 1925). The effect of fortuitous semantic changes (see footnote 7) also may have contributed to the definition of placebo as medicine.

Definition Limited to Inert Medicine

The first allusion to the placebo as inert occurred during the last decade of the 19th century. The details of this change and the possible happenstance contributing to it were described previously. Other factors were even more important: Contemporary scientific medicine began in the late 19th century (Shapiro, 1960a), and therapy became more rational and effective. Physicians probably became more confident, but, at the same time, somewhat selfconscious about their impotence and pretensions. The first Pure Food and Drug Act was passed in 1906 (Young, 1961). Polypharmacy was bitterly denounced, and senseless remedies decreased (Osler, 1905; Dubois, 1946; Young, 1961). Fewer medicines were available for simple psychological treatment and substances which were clearly inert could perhaps better perform this function. Psychological factors in illness and treatment became more evident following the remarkable success of Christian Science (Twain, 1899; Janet, 1925), the impact of homeopathy (Holmes, 1891), the study of hypnotism and suggestion, which was termed the stage of scientific psychotherapy by Janet (1924, 1925), and Bernheim (1889), and the introduction of moral, persuasive, suggestive, and insight psychotherapies that followed (Parker, 1908, 1909a, b). Perhaps a preference for uncontaminated or inert drugs developed in the belief that they differentiated their prescriber from the homeopathist. But the placebo was inert in this period by implication only. It did not become popularly or medically characterized as inert until about the second half of the 20th century.

Ironically, the major determinant of this limited definition was probably the recent introduction of scientific methodology in the evaluation of treatment and the conduct of clinical trials. This

development has been relatively sudden. Medical journals now publish more controlled than uncontrolled clinical studies.

Various controls, double blind procedures, and statistical analyses which were almost nonexistent prior to 1950, are commonplace today. It is too early to say whether this development will be considered by future historians as the major medical advance during the last decade (Bull, 1959; Klerman, 1961; Beecher, 1963).

Early in the development of controlled clinical trials inert placebos were given as single blind controls. This proved to be inadequate and the double blind procedure evolved as a more adequate method of controlling variables. The rationale was that the inert placebo, under double blind conditions, would control many of the psychological variables and permit clear-cut differentiation between active and inactive treatment (Modell and Houde, 1958; Nash, 1960; Shapiro, 1960a, 1961, 1963). Placebos have received considerable publicity through increased use in major studies such as the National Research Council study of tuberculosis in England from 1948 to 1955, the poliomyelitis study in America during the 1950's, and many studies of the placebo effect in recent years (Shapiro, 1960a, 1964c; Honigfeld, 1964). With these developments the placebo has become increasingly identified with inert substances.

Concurrent with these advances in methodology, clinicians and behavioral scientists became interested in the placebo phenomenon. Placebo literature, almost nonexistent previously, is now voluminous (Shapiro, 1960). More papers have probably been written about the placebo effect in the last eight years than in all previous years combined. The American Psychiatric Association held its first roundtable meeting on the placebo in 1959 (American Psychiatric Association, 1959); and many popular journals have reviewed the subject (Physicians Bulletin, 1955a, b; Spectrum, 1957a, b, 1960; Ubell, 1959; Rouché, 1960; Science Digest, 1961; S K & F Psychiatric Reporter, 1962; Medical Times, 1962; Hospital Focus, 1964; Medical Science, 1964). All contemporary dictionaries contain definitions of the placebo. But knowledge of treatment methodology and of the placebo effect has lagged behind developments of the past 10 years. For example, it now has become apparent that inert placebos frequently are inadequate controls in double blind studies. Inert placebos can be differentiated by patient and doctor, and the procedure may be

come a single or nonblind procedure. Incidental physiological effects of an active agent may have profound psychological effects on patients, physicians, and evaluators. Today it is known that an adequate placebo must often mimic many of the tell-tale effects of the active agent under study. This necessitates an active substance as a placebo control (Modell and Houde, 1958; Nash, 1960; Shapiro, 1960c, 1963, 1964a). The limited definitions that have recently appeared in dictionaries reflect this lag in knowledge.

Actually, the question of inert versus active placebo is academic, because there is no such thing as an inactive substance. For example, distilled water injections can cause hemolysis and water intoxication. Ingestion of two 5-grain capsules of sacchari lactis, QID, for 30 years, can result in a weight gain of 30 pounds, all other things being equal, so that even sugar can hardly be considered harmless, indifferent, or inert.

To differentiate between an active and inactive dosage of a drug is often difficult and arbitrary. Just as homeopaths of the past believed their dosages to be active, many physicians today unknowingly prescribe inactive dosages of tranquilizers, such as trifluoperazine, 1 mg. BID, or meprobamate, 200 mg. TID (Shapiro, 1964a). The inert-active continuum cannot be dichotomized. The dosage of many drugs is within a range in which it is difficult to specify when the drug is active or inactive, and when psychological factors and placebo effects become an important variable and determinant of drug response (Shapiro, 1963; 1964a).

The distinction between inert and active drug is not clarified by the definition of medicine, since it broadly includes "any substance or preparation used in treating disease, the science and art dealing with a prevention, cure or alleviation of disease, a science and art of restoring and preserving health which is the province of the physician" (Webster, 1933b).

Limiting the definition of placebo to inert medication is historically inaccurate, not in keeping with advanced modern usage, and an irrelevant, arbitrary, and heuristically useless concept; the practice should be discarded.

Psychotherapy in the Definition

Considering the long history of medicine, the history of the placebo is recent. The meaning and definition of placebo, as with most words, has changed during its brief history. There have

been periods in which the term was hardly used. Recently the *placebo* has become a popular word and an important methodological concept. It has replaced words like *suggestion* and *dummy preparation*. Revisions in the meaning and definition of placebo will probably continue to occur as a function of the changes in medical practice, knowledge, and theory.

This leads to the semantic question of whether new treatment methods should be included in the definition. The most recent treatments to be considered in the definition are psychotherapy and psychoanalysis. But psychotherapists frequently reject inclusion of these treatments. Their reactions are defensive, and similar to those of physicians and healers of the past when the effectiveness of therapeutic methods was challenged (Shapiro, 1960b). For example, when speaking to various groups about the placebo effect, the author has encountered many organically oriented psychiatrists who maintained that drug and convulsive treatment could not be placebos because active agents were used, although psychotherapy was thought to be a placebo treatment. Psychotherapists and psychoanalysts often considered drug and convulsive treatment to be placebo treatments, but frequently denied the possibility of psychological treatment being in the same category. Many surgeons include the aforementioned treatments in the definition but exclude surgery. Arguments against including psychological treatment in the definition include: Psychotherapy is not a drug and therefore cannot be a placebo. . . ; psychotherapy is the application of psychological principles, does what the placebo attempts to do unscientifically, and therefore is not a placebo. . . ; psychotherapy was not included in the original definition.

It is true that psychotherapy was not included in the original definition. But the reason for this exclusion is that no such treatment existed at the time. Retrospectively, however, it can be included because it is a *method* of treatment. More importantly, it can be operationally included in the definition as any therapy can and should be included. Not to include it would render logic and scientific methodology meaningless, and emphasize the essential defensiveness of such a position.

If a specific psychological therapy, tested under controlled conditions, resulted in nonspecific benefit no different from that resulting from nonspecific control therapies, it is incontestable that, as with a drug, any benefit would have to be attributed to what

is now referred to as the placebo effect. This operational definition has been advocated in many of the papers referred to in previous sections.

Distinction Between Placebo and Placebo Effect

It has been proposed that the placebo be defined as the agent or procedure and the placebo effect as the possible reaction (Fisher and Dlin, 1956; Lesse, 1962). The placebo effect may be positive (favorable response), or negative (unfavorable response), or absent (no response). This implies that the placebo is only used knowingly and deliberately, and the placebo effect, if it occurs, may be known or unknown to the prescriber of the placebo. Although this distinction has merit, it leads to a logical inconsistency. If a treatment is prescribed by a physician in the belief that it is specific and not a placebo, and a placebo effect occurs unknown to the physician, the treatment cannot then be considered a placebo treatment. This awkward inconsistency can be parsimoniously resolved by defining the placebo effect in terms of the placebo. It also can fulfill other historic and heuristic criteria.

Placebo Effect and Suggestion

A distinction should be made, however, between suggestion and the placebo. The terms *placebo* and *placebo* effect should be reserved primarily for therapies and therapeutic effects. *Suggestion* is associated more with laboratory experiments and hypnosis. There are historic, linguistic, and methodological reasons for this distinction. Important factors in the therapeutic situation are not present or are minimized in the experimental situation. These include an experimenter rather than a therapist, a subject rather than a patient, and a laboratory experiment rather than a clinical setting (Shapiro, 1960a, 1963, 1964c). Other factors include the physician-patient relationship, the physician's interest in the patient, and the clinical condition, professional and therapeutic commitments, optimistic needs of the physician, transference, counter-transference, patient expectations, clinical anxiety as distinct from experimental anxiety, and many other variables. In addition, there is little correlation between tests of suggestibility in a laboratory situation and the placebo effect in a clinical setting (Shapiro 1960a, 1963, 1964b, c).

Placebo Effect and Hypnosis

Autosuggestion and posthypnotic suggestion during hypnosis are included in the same category. However, if they are used as a therapeutic technique with expectations of therapeutic benefit, the procedure may be a placebo and result in placebo effects.

Placebos in Research

The term *placebo* has been reserved, however, for agents or procedures used as controls in experimental studies, whether or not the research includes evaluation of a therapy. British authors occasionally use the word *dummy* to describe an agent used as a control in research, and *placebo* to describe an agent used in therapy (Gaddum, 1954; Wilson 1962). The rationale for this differentiation is unconvincing (Beecher, 1956), and the word *dummy* is infrequently used in the literature.

Mechanism of Action in the Definition

Several authors have defined the placebo operationally by including explanatory mechanisms in the definition such as expectation, transference, conditioning, and so forth (Whitehorn, 1958; Hinse and Campbell, 1960, also see pp. 667-670). But none of the mechanisms has been experimentally verified as the major variable; an operational definition is therefore premature. Such definitions may have heuristic value, however, and provide models for further experimentation.

Proposed Definition of Placebo

A definition should be based on historic, linguistic, dynamic, and heuristic factors.

The original definition of placebo included medicines and methods. Therefore, all therapy was included in the first definition. Later, definitions became limited to medicine, and recently to inert substances. These changes paralleled changes in medical theory and practice. Recent advances in medicine and experimental methodology justify another revision in definition; it should now include any method of therapy. The definition should also provide a unified concept which operationally can include both physiologic and psychologic therapy. It should include active medication such as vitamins for neurasthenia (J.A.M.A., 1955), and surgical procedures such as mammary artery ligation for

angina pectoris (Wolf, 1959a, b; Beecher, 1961). Psychiatry is a new specialty; psychotherapy is a new treatment. This development in medicine should be reflected in the definition so that psychotherapy can also be included. Limiting the definition to its original literal meaning is unjustified historically, linguistically, and dynamically.

The placebo was used originally as a derisive epithet to describe the treatment of others and not knowingly or deliberately prescribed by physicians. Today, the criterion for placebo treatment is based on more than opinion. It is based on, or should be based on, principles of scientific methodology.

Other alternatives result in many difficulties. For example, a survey by the author (still in progress) has revealed many differences of opinion about the definition of placebo. Some believe that there is no such thing as a placebo. "If a placebo is prescribed by a physician because it is thought that it will help the patient, then it is specific and therefore not a placebo." Opinions vary from denying the existence of the placebo to including all therapy in the definition. The placebo tends to be defined so that its use is disavowed and projected onto others.

Many of the definitions seem to arise from the same motives that prompted Humpty Dumpty to say:

When I use a word...it means just
what I choose it to mean—neither more
nor less.

Lewis Carroll, 1832-1898

Inadequate definitions of the placebo and placebo effect can lead to erroneous conclusions and hamper research. For example, various investigators have attempted to relate placebo effects (positive, negative, and absent) to the personality of the patient. But these attempts have not been successful; personality traits found in one study differ from those reported in others. Contradictory findings are caused by many variables—e.g., different clinical conditions, patient populations, research procedures and settings. Some of these studies report, however, and it is commonly assumed, that placebo reactors—compared with non-reactors—are more anxious, hypochondriacal, dependent, inadequate, immature, impulsive, atypical, depressed, religious and stereotypic. Reactors are thought to be unintelligent, uneducated, frequently neurotic or psychotic, more frequently female, from a

deprived social class, and so forth (Shapiro, 1964b, c).³¹ These personality variables probably describe patients for whom a placebo in the form of a drug is culturally appropriate. The traits are probably not inherent in placebo reactors, but in patients who are drug-oriented. Such patients may react favorably to a drug placebo stimulus and unfavorably, or not react, to a psychotherapeutic placebo stimulus. The converse may occur with patients who believe in psychotherapy. They may not react, or may react adversely, to a drug placebo stimulus. In other words, a drug may be a good placebo stimulus for some patients; psychotherapy may be a good placebo stimulus for other patients (Schmideberg, 1928; Fenichel, 1954; Shapiro, 1964b, d).

All patients are likely to react occasionally to placebos if the placebo stimulus is appropriate; in other words, placebo proneness is universal. Recognizing the importance of this stimulus variable is a precondition for study of the placebo effect (Shapiro, 1964b, c, d). If research on the placebo effect is limited to drugs, the underlying mechanism may be obfuscated, and the secret of the placebo reactor may continue to elude us. A heuristic definition can minimize that possibility.³²

The conceptual schema for the author's definition of placebo is illustrated in Figure 1. It illustrates how various factors may contribute to therapeutic results. The vertical axis represents the total effectiveness of a treatment. The ordinate represents the ratio of placebo and nonplacebo factors in treatment. These terms are equivalent to nonspecific and specific effects. The arrow illustrates the potential interaction between placebo and nonplacebo factors. Not included in the schema are factors such as fluctuations in the natural course of illness, clinical bias, methodological vari-

³¹Attributing these traits to the placebo reactor may be a sophisticated projection or rationalization of feelings about patients who are given or respond to placebos.

³²The first attempt to identify the personality of the placebo reactor occurred ten years ago in studies by Lasagna and others (Lasagna et al., 1954, von Felsinger et al., 1955, Lasagna 1956). These have been extensively quoted and have stimulated other such studies. But they also contributed to the myth of the placebo personality and sidetracked fruitful research for many years. These studies can be criticized on many levels: atypical populations, limited settings, inadequate numbers, many uncontrolled variables, anecdotal and insufficient data, extensive generalizations unwarranted by the data, and so forth (see also Trouton, 1957). Since methodology has improved so much in the past ten years, the shortcomings of these studies are understandable. Incomprehensible, however, is the continued presentation of these unwarranted generalizations in recent papers (Lieberman, 1962; Lasagna, 1963).

ables, untoward side effects, negative placebo effects, and so forth.

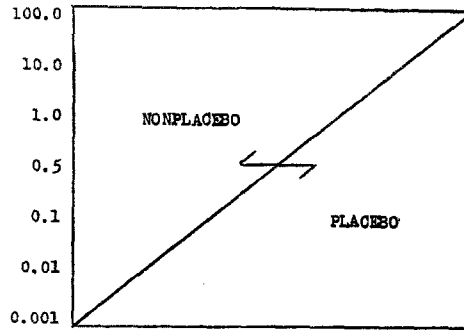


Figure 1. Therapeutic Effect: The ratio of placebo and nonplacebo factors in the effectiveness of therapy (e.g., grams chlorpromazine)

The concept can be illustrated by considering the potential effects on a patient of increasing dosages of intravenous chlorpromazine. As illustrated in Figure 1, the dosage of chlorpromazine can vary from 0.001 to 100.0 gm, or 1.0 to 100,000 mgm. The ratio of placebo and nonplacebo effects will vary as a function of dosage. Only placebo effects will occur with homeopathic dosages of 1.0 mgm. of chlorpromazine. The ratio of nonplacebo, specific, and predictable effects will increase with higher dosages. As the dosage is increased the drug will cause sedation, hypnosis, anesthesia, coma, and finally death.

The most predictable and highly specific effects will occur with a massive overdose of chlorpromazine. At that dosage the cortex cannot function. Without a functioning cortex, non-specific, placebo, or psychological effects do not occur. For example, if therapeutic dosages of atropine are given to a decorticate subject, the effects on the gastrointestinal mucosa are specific and predictable. The same dosages given to a subject with an intact cortex will have variable effects which will be related to the subject's psychological state (Wolf, 1959). Most therapeutic agents and procedures are used in subjects with intact cortices, and are useful only in a range in which psychological factors are important. Therefore, placebo and nonspecific effects are an almost inevitable concomitant of all therapy.

This schema can probably be applied to every therapeutic modality. It would include treatment with drugs such as barbit-

urates, digitalis, thyroid, and vitamins, as well as surgical treatment, psychotherapy, psychoanalysis, and so forth.

The author's proposed definition makes no assumption about which treatments are placebos, or about the mechanism of placebo action. These issues are left open because the placebo effect is a multi-determined phenomenon which is not yet understood (Shapiro, 1964b, c; Honigfeld, 1964a, b). The definition is a phenomenological statement which avoids becoming tautological. It provides a good model for research, a structure into which variables can be put for testing, and makes possible independent assessment about which everyone can agree.

The author believes that the definition which follows fulfills these criteria:

A placebo is defined as any therapy (or that component of any therapy) that is deliberately used for its nonspecific psychologic or psychophysiologic effect, or that is used for its presumed specific effect on a patient, symptom, or illness, but which unknown to therapist and patient is without specific activity for the condition being treated.

A placebo, when used as a control in experimental studies, is defined as a substance or procedure that is without specific activity for the condition being evaluated.

The *placebo effect* is defined as the nonspecific psychologic or psychophysiologic effect produced by a placebo.

In other words, a therapy may be used with or without knowledge that it is a placebo. It would include treatments given in the belief that they were not placebos, but which actually are placebos by objective evaluation. The placebo may be inert or active and may include, therefore, all medical treatment no matter how potentially specific or how administered. It may take the form of oral and parenteral medication, topical preparations, inhalants, and all mechanical, surgical, psychotherapeutic, and other therapeutic techniques. It would include a treatment that produced symptoms or side effects which were not specific for that treatment. A placebo may or may not result in a placebo effect, and the effect may be favorable or unfavorable—that is, positive or negative.

Examples of a placebo would be the use of homeopathic dosages of digitalis for psychoneurotic anxiety, hysterectomy for irritable

colon, or 5 mg. of chlorpromazine for an acute psychosis. Examples of nonplacebos would be penicillin for scarlatina, digitalis for congestive heart failure, and appendectomy for appendicitis.

CONCLUSION

Although the definition proposed in this paper may in the future prove to be too inclusive, for heuristic reasons it would be premature at the present time to make specific exclusions. It is likely that various placebogenic factors will be reliably isolated in the future, factors such as remission and exacerbation during the natural course of illness, observer bias and effects of investigators, other methodological variables, patient expectations, and so forth. When everything is known about the placebo and placebo effect, there will probably no longer be a need for the definition, except in etymologies of obsolete terms, but this is a desideratum for the future.

SUMMARY

With increased interest in the placebo effect and clinical methodology, definitions of the placebo have proliferated. But there is little agreement among lexicographers, historians, clinicians, and researchers about how to define this word.

Derivations of the word *placebo* from the Hebrew and Latin and its use in the Bible and literature were reviewed. Historical inaccuracies in classical references to the placebo's origin, history, and development were corrected. An explanation was given for the introduction of the word in 1785, and for the changes in definition that have appeared since that time. Definitions of the placebo and placebo effect, based on historic considerations and heuristic principles, were then proposed.

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