penicillin, which is unpatented and not highly advertised, and the broad spectrum antibiotics. Within its range of activity, penicillin is usually more potent than the broad spectrum drugs.[71] But micro-organisms tend to become resistant to certain antibiotics; many of the newer antibiotics are said to be effective against strains resistant to the older ones. Among the broad spectrum drugs, chloramphenical may currently be regarded as somewhat distinct from the others, in that fewer strains have become resistant to it, and for two reasons. First, the use of chloramphenicol was discouraged to some extent in the early 1950's when publicity was given to the incidence of its lethal side-effects; hence its less frequent use during that period provided less occasion for the development of resistant strains. Second, this drug resembles penicillin more than do the other broad-spectrum antibiotics in that microorganisms do not easily develop resistance to it;[72] chloramphenicol is, in fact, the most lethal of the broad spectrum antibiotics to micro-organism and patient alike.[73] The incidence of side effects is often more important than the spectrum of primary efficacy of the antibiotic as far as drug demand is concerned. Advertising may influence prescription demand by stressing the alleged absence of side effects as well as therapeutic efficacy. The absence of any advertising may conversely prevent the wide-scale use of extremely efficacious antibiotics. Bacitracin is a case in point. The drug is so free of side effects that some of its preparations may be bought over the counter. The patent is owned by the federal government, and royalty-free licenses may be obtained. The only ethical drug firm currently producing this drug, Pfizer, also sells its own patented antibiotics, tetracycline and oxytetracycline, and does no sales promotion for bacitracin, save of a negative sort. Originally the Food and Drug Administration restricted its use to hospitals, but later removed the restriction, but as of September, 1960, Pfizer (despite protests from the discoverer of the drug) continued to print the former restriction on bacitracin labels and brochures.[74]

C. Product competition in individual drug markets

The earliest of the corticosteroids, cortisone, was first synthesized in 1944 by Merck, and commercial production began in 1948.[75] The drug first proved its effectiveness in relieving the symptoms of rheumatoid arthritis and related clinical syndromes, although concomitant side effects presented complications. Cortisone is a naturally occurring substance in the human body (adrenal cortex) and no product patent could be obtained. Process patents presented no real barrier to entry, and Merck soon had competition from a number of large and small firms.[76]

Squibb discovered fludrocortisone in 1953, by modifying the hydrocortisone molecule. Squibb obtained a patent, sells the drug under the name "Florinef" and has apparently licensed no other sellers. More potent than its parent, its side effects are also more severe.[77]

Prednisone was the next corticosteroid to be found, along with the related compound prednisolone. These discoveries are credited to the Syntex Corporation of Mexico in 1955. By nature still further modifications of the cortisone molecule, they are generally felt to constitute some actual improvement over the parent substance. They are used to treat the same disorders, and have about five times the antirheumatic activity of the parent steroids.[78] No patent has yet been awarded for either drug, and several large firms and many small firms sell both drugs.

Some medical authorities hold that no essential advances have been made in the corticosteroids field since prednisone and prenisolone were introduced. Upjohn found methylprednisolone in 1957 as a further modification of the pred-

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[71] L. S. Goodman & E. Gillman, The Pharmacological Basis of Therapeutics 1322–23 (1956).

[72] Testimony of Dr. Maxwell Finland of Harvard University, Hearings on Administered Prices, pt. 24, 13947–49.

[73] In a nation-wide survey of all severe antibiotic reactions from late 1953 to early 1957, 25 deaths from severe skin reactions and blood duscrasias were associated with the use of chloramphenicol, and only two deaths from the same causes were associated with the use of the tetracyclines. L. Meyler, Side Effects of Drugs 129–30 (1960).

[74] Testimony of Dr. F. L. Meleney of the University of Miami, Hearings on Administered Prices, pt. 24, at 14195.

[75] Testimony of Dr. E. C. Kendall of Merck, *id.*, pt. 14, at 8018–20.

[76] Testimony of J. T. Connor, president of Merck, *id.*, pt. 14, at 8025–26.

[77] Modern Drug Encyclopedia and Therapeutic Index 471 (E. P. Jordan ed. 1958).

[78] Meyler, *op. cit. supra* note 73, at 148.