FIFTY YEARS OF PROGRESS AS SHOWN BY VITAL STATISTICS

BY

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The Registrar-General's Annual Report for 1898 tells us that in a population of about 31½ millions in England and Wales there occurred 552,141 deaths, of which 86,755 were attributed to "zymotic" diseases. Fifty years later, in 1948, the population had increased by 12 millions but the number of deaths was actually smaller by 82,243, giving a crude death rate of 10.8 per 1,000 compared with 17.6. The group of diseases called "zymotic" in 1898 produced only 7,490 deaths in 1948, and their contribution to the total death rate fell from 2.76 per 1,000 living to 0.17, or one-sixteenth of its value 50 years before. From all other causes the total deaths were almost the same in the two years despite the great increase in population.

Indices of Progress

Crude death rates have ceased to be reliable indices of the improvement in healthiness of the people since the first world war, the reason being that the cumulative effect of falling births and declining death rates among young people began to produce a rapid rise in the proportion of elderly people in the population. In 1901 the number of persons aged 65 and over in each thousand was 47, and in 1921 it was 60, but by 1947 it had increased to 105; and since the old necessarily die at a much greater rate than the young this has had the effect of keeping the crude death rate at all ages almost constant at about 12.2 notwithstanding a progressive fall in death rates at every age.

The comparative mortality index, which corrects for changes in the population structure and expresses mortality in terms of that in 1938 as unit, gives the best general indication by a single figure of the effects of hygienic and therapeutic advances in keeping people alive longer. These indices are shown in Table I, together with the infant mortality rate and death rates at ages 5-10 and 55-65.

TABLE I.—*Indices of Mortality from All Causes in England and Wales, 1896-1900, 1921-30, 1938, and 1948*

	1896-1900	1921-30	1938	1948	1948 as Percentage of 1896-1900
Comparative mortality at all ages M F	1.825 1.951	1.163 1.224	1.000 1.000	0.815 0.789	45 40
Infant mortality per 1,000 live births	156	72	53	34	22
Death rate at ages 5-10 per 1,000	4.12	2.42	1.87	0.75	18
Death rate at 55-65 per 1,000 M F	34.1 27.4	24.6 18.3	23.1 15.5	21.6 12.2	63 45

The death rates of infants and of children aged 5-10 are about one-fifth of what they were half a century ago. Out of 100,000 females of all ages living in 1938, 1,083 died in the year, and after allowing for changes in age distribution of the population the corresponding number in 1948 was 855. This is comparable to an annual average of 2,114 at the mortality rates current in the period 1896-1900. That is what is implied by saying that their comparative mortality index is now only 40% of what it then was. In other words, to every two females now dying in a year there would have been added three more half a century ago, supposing the populations to have been of the same size and of the same age distribution. For males the improvement has not been quite so great: to every nine males now dying in a year 11 more would have been added.

Death Rates by Sex and Age

The ratio of male to female mortality at all ages, adjusted to allow for the differences between the age distributions of the male and female populations, has tended to rise throughout the past century. In 1846-50 it was 1.088, indicating an average male excess, age for age, of 9%; in 1896-1900 it was 1.178, the excess having increased to 18%. By 1931-5 it was 1.276, and in 1947 it was 1.389, representing a male excess of 39%. The ratios of male to female death rate at successive age groups in 1896-1900 and 1948 are shown in Table II.

TABLE II.—*Ratio of Male to Female Death Rate and Relative Decrease in Mortality of Each Sex*

Age Group	Ratio of Male to Female Death Rate		Decrease in Death Rate (% of Initial Rate) from 1896-1900 to 1948	
	1896-1900	1948	Males	Females
0-	1.18	1.28	84	86
5-	0.99	1.42	78	85
10-	0.97	1.16	72	77
15-	1.07	1.16	64	67
20-	1.18	0.99	69	62
25-	1.15	1.06	71	69
35-	1.22	1.29	72	73
45-	1.29	1.55	55	63
55-	1.24	1.77	37	55
65-	1.17	1.63	28	45
75-	1.13	1.28	24	33
85 and over	1.09	1.15	26	29

The magnitude of the proportionate fall in death rate of females during the 50 years diminished with advancing age from about 85% for young girls to 62% at 20-25, then increased again to 73% at 35-45, after which it decreased regularly to 29% for the very old. It is often stated that the death rates of elderly people have not changed appreciably, and the further deduction is made that they are not likely to fall much in the next half-century; but neither the statement nor the deduction can be supported by the figures. It is true that during the latter half of the nineteenth century death rates of females at ages over 55 changed little, although they were falling all the time at ages before 35, and began to fall after 1875 at 35-45 and after 1895 at 45-55. From the beginning of the present century, however, the rates for each age group over 55 began to fall, and the improvement in the 50 years has been very considerable, mortality between 55 and 75 having been halved, whilst at ages over 75 it has been reduced by one-third. Appreciation of this is important, because nearly a quarter of the present female population is aged 55 and over, and the amount of increase to be anticipated in that proportion during the next 50 years depends a good deal upon the trend of their death rates.

The story has been similar for males, but with certain differences. The death rate of boys of school age fell by 75% compared with 81% for girls; and at ages between 45 and 85 the rate of improvement has been substantially less among men than among women, as shown in Table II. As a result the male death rate is now more than one and a half times the female rate for each age group between 45 and 75. This is in the main an aftermath of the first world war, removing as it did so many of the healthiest men from these groups, who in 1918 were between the ages of 15 and 45, and exposing others to hardships greater than were suffered by women of similar age. In the age group 55-65 particularly, male survival has failed to improve as quickly as that of females, with consequent increase in the mortality sex-ratio at that age from 1.24 in 1896-1900 to 1.49 in 1938 and to 1.77 in 1948. The large increase in this ratio during the period of the second world war is connected with the fact that these men were aged 21-30 in 1914. They represent the survivors of those bearing the

brunt of the first world war, who were then subjected again to exceptional stresses as civilians in the second war.

Life Expectation

Expected survival according to life tables provides another useful index of improvement, and Table III compares the position in 1945 with that 50 years before, in 1891-1900 (according to English Life Table No. 6).

TABLE III.—*Probabilities of Attaining Certain Ages and Expectations of Life According to the Mortality Rates of 1891-1900 and 1945*

	Males		Females	
	1891-1900	1945	1891-1900	1945
Survivors out of 1,000 born, expected to reach				
Age 5	750	938	782	951
15	725	927	756	942
45	577	825	619	880
65	332	599	398	725
75	159	355	211	505
Expectation of life at				
Birth	44.1	62.6	47.8	68.6
Age 1	52.2	64.9	54.5	70.4
40	25.6	31.1	27.8	35.0
60	12.9	15.4	14.1	18.1

Survival of children to their fifth birthday is now about 95 out of 100, having improved further since 1945, but at the end of the last century no more than 76 were reaching that age. According to the death rates of that period four out of ten girls and one out of three boys could expect to live to 65, assuming that the death rates remained constant, which is what a life table implies. The prospects are now very different, for seven girls and six boys out of ten being born can expect to reach 65 even if no further fall in death rates occurs. Indeed, half the girls now being born may expect to attain the age of 75.

The expectation of life expresses this in a different way as the mean duration of life to be anticipated by infants just born or by people who have just attained a particular age, on the assumption that death rates will not change. During the 50 years the expectation at birth has improved by 18½ years for boys and by 21 years for girls. Infants who survive the dangers of the first year have a longer expectation of life than those who have just been born, and in 1945 girls attaining their first birthday had an expectation of living another 70 years, the corresponding figure for boys being 65 years. These expectations were 16 and 12 years better than those of 1891-1900. At his 40th birthday a man may now expect to live another 31 years, an improvement of five and a half years; and a woman of 40 may expect to live 35 years, an increase of seven years. Even at 60 a woman's expectation of further life has improved by four years during the half-century.

Infant Mortality

The rate of mortality in the first year of life has always been regarded as a good index of progress in hygienic conditions within a community, although from some points of view the second year of life gives a better index. It is not easy, however, to obtain the death rates in the second year 50 years ago, and for many countries' second-year rates are not ascertainable even at the present time. Infant mortality rates from all causes as given in official reports of a number of countries for various periods from 1901-5 up to 1948 are shown in Table IV. Some of these rates are not precisely comparable with those of England and Wales owing to exclusion of deaths of infants occurring soon after birth, but in recent years improvements in registration have eliminated many of these faults. The rates for France and those for Belgium up to 1935 are too low on this account. All rates for 1941-5 are arithmetical means of the five annual rates.

TABLE IV.—*Infant Mortality at Ages under 1 Year per 1,000 Live Births in Various Countries*

Country	1901-5	1911-15	1921-5	1931-5	1941-5	1946	1947	1948
England and Wales	138	110	76	62	50	43	41	34
Scotland	120	113	92	81	68	54	56	45
Northern Ireland ..	—	102	82	78	73	54	53	46
Australia	97	70	58	41	35	29	29	28
Canada	—	—	98	75	55	47	45	44
New Zealand	75	54	43	32	30	26	25	22
Belgium	148	—	100	82	87	71	64	55
France	149*	—	95	73	81	73	67	51
Italy	167	140	127	105	108	84	82	70
Netherlands	136	—	69	144	50†	42	33	29
Sweden	85†	—	60	50	31	26	25	22
U.S.A.	—	—	74	59	41	34	32	32

* 1896-1905. † 1901-10. ‡ Average 43 in 1941-4, but 79 in 1945.

The ranking of these countries according to their infant mortality has remained remarkably constant, Italy, France, Belgium, and Canada having higher rates than England and Wales, whilst the U.S.A., Sweden, Netherlands, Australia, and New Zealand had lower rates. Scotland and Northern Ireland also had lower rates early in the century, but subsequent improvements have not kept pace with those in England and Wales. This table of progress since 1901-5 lends no support to the idea that limits can be set to further reductions of infant mortality attainable in the future. During 50 years the English rate has been halved twice over.

Stillbirths have been registered for 20 years only, but during that period the combined stillbirth and neonatal death rate per 1,000 total births has fallen from 70 in 1928 to 42 in 1948, or by 40%. In the same period infant mortality at ages 1-12 months fell from 34 to 14, or by 59%. It is no longer true, therefore, that the decline in infant wastage round about birth is lagging very much behind the improvement in later infancy.

Causes of Death

The zymotic diseases, to which 86,755 deaths were attributed in 1898, are shown in Table V, with the corresponding numbers of deaths in 1948 as nearly as changes in nomenclature permit such comparison. The causes are arranged

TABLE V.—*Deaths from "Zymotic" Diseases in 1898, with Corresponding Numbers in 1948*

Cause of Death as Described in 1898	Number of Deaths		Death Rates per Million	
	1898	1948	1898	1948
Miasmatic:				
Measles and rubella	13,260	329	422	8
Influenza	10,405	1,240	331	29
Whooping-cough	10,175	748	324	17
Diphtheria	7,661	156	244	4
Enteric fever	5,708	48	182	1
Scarlet fever	3,548	36	113	1
Smallpox	253	0	8	0
Chicken-pox	116	10	4	0.2
Typhus	47	0	1	0
Mumps	59	16	2	0.4
Cerebrospinal fever	11	300	0.4	7
Other miasmatic illnesses*	166	—	5	—
Diarrhoeal:				
Cholera, diarrhoea, and dysentery	30,096	3,131	959	72
Malarial	91	11	3	0.3
Zoogenous:				
Cowpox, vaccination effects ..	26	5	0.8	0.1
Anthrax, splenic fever	18	1	0.6	0
Hydrophobia, glanders	6	0	0.2	0
Venereal:				
Syphilis (not including G.P.I., tabes, aneurysm)	1,801	705	57	16
Gonorrhoea, stricture of urethra ..	335	183	11	4
Septic:				
Puerperal fever	1,707	187	54	4
Erysipelas	970	51	31	1
Pyæmia, septicaemia	251	193	8	4
Phagedæna	45	140†	1	3
Total	86,755	7,490	2,763	172

*Mainly ill-defined fevers. † Cellulitis, acute abscess.

in descending order of their frequency within each of the groups used in 1898.

The table speaks for itself. The one cause showing a noteworthy increase is cerebrospinal fever, only 11 deaths from which were recognized in 1898; but there were 7,556 deaths attributed to "inflammation of the brain and meninges" compared with about 700 in 1948, so this apparent anomaly is almost certainly to be explained by better diagnosis of the meningococcal infections. Cholera had 1,103 deaths assigned to it in 1898; but how many of this total were true cholera is doubtful, and they have been grouped with deaths from dysentery and diarrhoea of unspecified cause. For uniformity with the other causes in the table the puerperal fever rates have been based on the total population.

Amongst the reasons for the extraordinary reduction in the death rate from this group of "zymotic" diseases by 94% must have been:

(a) Improvements in water supplies and sanitation, virtually eliminating cholera and enteric fever and contributing to the great reduction in other diarrhoeal diseases.

(b) Decline in virulence or increase in natural immunity—e.g., scarlet fever, influenza.

(c) Protection of the community by public health measures against infection—e.g., diphtheria, smallpox, typhus, anthrax, malaria, hydrophobia.

(d) Improvements in personal hygiene, education, housing, and medical care resulting in reduced fatality—e.g., measles, whooping-cough, diphtheria.

(e) New discoveries in chemotherapy, reducing fatality from streptococcal diseases, puerperal fever, venereal diseases, and complications of measles and whooping-cough.

The respective contributions of these to the total improvement for this group of causes of death cannot be estimated except where powerful measures were introduced rapidly and on a large scale, as in the case of the sulphonamides and penicillin, which began to affect death rates appreciably in 1937 and 1945 respectively. In Table VI the trend of

TABLE VI.—Crude Death Rates Per Million Females from Causes Mainly Due to *Streptococcus* and *Pneumococcus*. Puerperal Sepsis Rate. 1928-47

Cause Group	1928-30	1935	1936	1939	1942	1945	1946	1947
Puerperal sepsis (excluding abortion) per 100,000 live and still births ..	154	134	118	63	42	24	18	16
Scarlet fever, erysipelas, septicaemia, cellulitis ..	62	58	54	27	19	17	12	10
Ear and mastoid disease ..	30	29	29	23	17	17	15	14
Appendicitis, peritonitis, cholecystitis ..	106	116	113	97	71	61	57	52
Lobar pneumonia ..	203	174	177	126	106	91	90	91
Acute bacterial endocarditis ..	23	26	24	23	23	14	12	11

mortality of females since 1928-30 is shown from several groups of diseases (some not included in the zymotic diseases) for which those drugs have been beneficial.

Mortality from the first two groups was being affected by other causes before 1937, and the downward trend was then greatly accelerated. For the next three groups mortality was not changing consistently (the high rate for lobar pneumonia in 1928-30 being due to the very exceptional year 1929), but it began to fall after 1936. Bacterial endocarditis showed no fall until the advent of penicillin.

In 1898 the deaths assigned to tuberculosis (including "tabes mesenterica") totalled 60,139, and in 1948 tuberculosis deaths were 21,983. The comparative mortality index for the period 1896-1900 was 3.125 and in 1948 it was 0.826, indicating a reduction of 74% when allowance

is made for changes in age distribution of the population and changes in classification.

Deaths from violent causes numbered 20,278 in 1898 and 18,716 in 1948. The crude death rate from accidents caused by vehicles and horses in 1898 was 84 per million, and the rate attributed to road transport in 1948 was 92 per million, a very small increase when the advent of motor road vehicles is considered. For burns and scalds the rate fell from 74 to 14 per million; and for all other forms of violence it decreased from 488 to 324 per million.

For all causes of death other than the zymotic diseases, tuberculosis, and violence the death rate was 12.3 per 1,000 in 1898 and 9.7 in 1948.

Certificates of Cause of Death as Instruments of Research

There is sometimes a tendency to decry the death certificate as an imperfect source of knowledge, and to suggest that in some Utopian future morbidity records will be available of such precision that it will be possible to consign death certificates to the rubbish heap of outworn instruments. For such an idea there is at present no vestige of probability, notwithstanding the fact that 1950 sees the emergence on the scene of the first comprehensive International Statistical Classification of Diseases, Injuries, and Causes of Death. That morbidity statistics will make greater contributions than in the past to public health and research, both national and international, is beyond question; but, if only because the average person consults his doctor some 300 times but dies only once, they are not likely to supplant mortality statistics.

The present somewhat cynical notion that causes of death after 65 are not of great importance can be only a passing phase. Lengthening of the average span of life has proceeded so rapidly that we have not yet grasped all that is implied by the expectation that half the girls now being born will live to 75 and half the boys to 70. With a readjustment of values, preservation of a life at 70 will take its rightful place as no less important than was the saving of a life at 50 half a century ago; and causes of death at advanced ages will demand more careful attention than is given to them at present.

This will be no easy task for the doctors who have to certify deaths, for a study of present certificates shows how complex the certification of causes at advanced ages is becoming. Amongst the young a single cause of death often suffices to tell the story, but in later life that is generally not true; and the conscientious certifier must endeavour to set out in logical order a combination of conditions which eventually culminated in death. Writing in 1887 on "Fifty Years of Civil Registration" in the 50th Annual Report, the Registrar-General said: "There is still also much occasion for the exhortation addressed by the Presidents of the Colleges of Physicians and of Surgeons that they should give such certificates of causes of death as might further the advance of medical science. . . ." This is still true to-day, though great credit is due to the large majority of doctors for their manifestly sincere efforts to obey that exhortation of more than a century ago.

The reason why some 14,000 inquiries for clarification or fuller information concerning certified causes need to be sent annually is partly because of the increasing detail of classification demanded by the users of medical statistics—that is to say, by the medical profession itself. Large numbers of certificates, however, are still filled in without due regard to the instructions provided, and in the text volume of the Statistical Review for 1940-5 (pages 81-83) the Registrar-General has called attention to defects in certification and how many of them could be avoided.

Rutherford Morison operating in the old Royal Infirmary, Newcastle-upon-Tyne, 1906

University College Hospital—nearly fifty years later

Tracing made by
Willem Einthoven,
1904

Brit. med. J.
1912, 1, 1421

ELECTRO-CARDIOGRAPHY AND ITS IMPORTANCE IN THE CLINICAL EXAMINATION OF HEART AFFECTIONS.

By THOMAS LEWIS, M.D., M.R.C.P.*

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MEDICAL SCHOOL; PHYSICIAN TO OUT-PATIENTS,
CITY OF LONDON HOSPITAL.

PART I.

The Method Employed in Obtaining Electro-cardiograms.
The electro-cardiographic method is one by means of which curves are obtained of electric changes which result in the body from the activity of the heart's muscle. The installation required for this work comprises a sensitive galvanometer and its accessory switchboards, and an arc light and camera.

The galvanometer used for the purpose is a peculiarly sensitive one; it is composed of a heavy electro-magnet the poles of which are close together.

A landmark in clinical medicine, 1912

Mackenzie's polygraph and a tracing, 1903

E.C.G. by Thomas Lewis, about 1911

Direct-writing electrocardiography, 1949

Electroencephalograph

Electromyograph

E.E.G. of a boy with petit mal

E.M.G. showing effect of muscle contraction against resistance

Department of Physiology, Middlesex Hospital Medical School, 1949

× 1,000

Staph. pyogenes aureus. Rosenbach, 1884

Microscope, 1900

× 370

M. tuberculosis. Koch, 1882

× 15,000

Staph. aureus, left;
tubercle bacillus,
right. Shown by
electron micro-
scope.

× 45,000

Influenza virus, Smith, Andrewes, and
Laidlaw, 1933

Virus on avian red cell : × 10,000

EM3 electron microscope, 1948

Bact. coli. Escherich, 1885

× 15,000

1934—Parathyrotropic

1932—Lactogenic

1933—Pancreatropic

1933—Adrenocorticotropic

1927—Gonadotropic

1929—Thyrotropic

Oxytocin

Vasopressin

1928

Diabetogenic—1931

Growth—1921

Ketogenic—1930

NOTE ON THE TREATMENT OF MYXŒDEMA BY HYPODERMIC INJECTIONS OF AN EXTRACT OF THE THYROID GLAND OF A SHEEP.

Read in the Section of Therapeutics at the Annual Meeting of the British Medical Association held in Bournemouth, July, 1891.

By GEORGE R. MURRAY, B.A., M.B.CAMB., M.R.C.P.LOND., Newcastle-on-Tyne.

MYXŒDEMA has until recently been considered an incurable disease. Since the pathology of this remarkable condition, however, has become more fully understood, hopes of the possibility of greatly relieving the symptoms, if not of curing the disease entirely, have been entertained. The observations of the thyroid gland in which

British Medical Journal, 1891, 2, 796

Desoxycortone, 1936

XXXIX. CHEMISTRY OF THYROXINE.

I. ISOLATION OF THYROXINE FROM THE THYROID GLAND.

By CHARLES ROBERT HARINGTON.

From the Department of Pathological Chemistry, University College Hospital Medical School, London.

(Received February 16th, 1926.)

In 1919 Kendall [1919, 1] announced, as the result of a long and painstaking investigation, the successful isolation from the thyroid gland of a crystalline substance containing 65% of iodine, which he named "thyroxin," and which has been proved by numerous clinical investigations [Boothby and Sandiford, 1924] to be the substance, or at least one of the most important substances, through which the thyroid gland exerts its control of the metabolic rate. Subsequently Kendall [1919, 2] published a second paper in which the empirical

Biochemical Journal, 1926, 20, 293

THE AMERICAN JOURNAL OF PHARMACY

NOVEMBER, 1901.

ADRENALIN THE ACTIVE PRINCIPLE OF THE SUPRARENAL GLANDS AND ITS MODE OF PREPARATION.

By Dr. JOKICHI TAKAMINE.

I have no doubt that a good many of you present have read an account of adrenalin and some of you no doubt have

Takamine, 1901

CHEMICAL STUDIES OF THE SUPRARENAL CORTEX

IV. STRUCTURES OF COMPOUNDS C, D, E, F, AND G

By HAROLD L. MASON, WILLARD M. HOEHN, AND EDWARD C. KENDALL

(From the Section on Biochemistry, The Mayo Foundation, Rochester, Minnesota)

(Received for publication, March 11, 1938)

The isolation and properties of two series of compounds separated from the suprarenal cortex have been given in previous papers (1-5). The structures of Compounds A, B, and H which make up the C₂₇O₂ series have been described, and in this paper the probable structures of Compounds C, D, E, F, and G which constitute the C₂₇O₂ series are discussed. Compound D was assigned only 20

J. biol. Chem., 1938, 124, 459

Aus der Klinik Scheute in Wien
Zur Physiologie und Pathologie der Ovarialfunktion.
Von
Dr. Ludwig Adler,
Assistent an der Klinik.

Follicular hormone. Adler, Arch. Gynäk., 1912, 95, 349

Oestrone, 1929
Progesterone, 1934

AN OVARIAN HORMONE

PRELIMINARY REPORT ON ITS LOCALIZATION, EXTRACTION AND PARTIAL PURIFICATION, AND ACTION IN TEST ANIMALS *

EDGAR ALLEN, Ph.D.

AND EDWARD A. DOISY, Ph.D.

ST. LOUIS

The fact that double ovariectomy abolishes the cyclic changes which normally occur in the genital tract of female mammals demonstrates that these changes are due to some influence from the ovaries. That this

J. Amer. med. Ass., 1923, 81, 819

THE EXTRACTION OF A PARATHYROID HORMONE WHICH WILL PREVENT OR CONTROL PARATHYROID TETANY AND WHICH REGULATES THE LEVEL OF BLOOD CALCIUM.*

By J. B. COLLIP.

(From the Department of Biochemistry, University of Alberta, Edmonton, Alberta, Canada.)

(Received for publication, December 3, 1924.)

INTRODUCTION.

The communication represents the preliminary results of a direct attack upon the problem of the suggested hormonal function of the parathyroid glands. The literature on the parathyroid glands

J. biol. Chem., 1925, 63, 395

73. The preparation of an active extract of the suprarenal cortex. J. J. Pflüger and W. W. Swingle, Princeton University.

The preparation of a physiologically active extract of suprarenal cortex has been reported by Bogoff and also by Hartmann. The former has given no details, while the latter uses water as the extracting media. The extract reported here is to our knowledge the first potent extract of suprarenal cortex to be prepared by means of organic solvents. The suprarenal glands (beef) packed in ice are received from the slaughterhouse within twenty-four hours after the death of the animals, and the cortex dissected as free as possible from extraneous fat and medullary tissue. The ground cortical tissue is first extracted at room temperature from twenty-four to forty-eight hours with 95 per cent alcohol and then with 80 per cent alcohol. The extractives are concentrated separately in partial vacuo at a low temperature and the residues extracted with benzene. The benzene is removed in a similar manner and the lipid residue freed from the last traces of benzene with absolute alcohol. The residue is dissolved in corn oil and administered subcutaneously. One cubic centimeter of the finished extract is equivalent to 30 mgms of fresh adrenal

Anat. Rec., 1929, 44, 225.

Pflüger and Swingle describe the preparation of the first potent extract of suprarenal cortex, 1929

Gestrogenic Activity of Certain Synthetic Compounds

In earlier communications^{1,2} two of us have described the estrogenic activity of certain derivatives of diphenylethane, and in particular it was shown that the introduction of an ethylene linkage between the α and β carbon atoms of the diphenylethane moiety greatly increased the potency of the derivatives were found.

Following up this of hydroxypropylbenzer compounds with the

colourless plates, alcohol; diacetate, similar after crystallization

The substances, th above, have all been su

the results are in

ations.

... DODDS. L. GOLDBERG. Middlesex Hospital, W.1. W. LAWSON. Guyon Perrins Laboratory, University, Oxford.

... and Lawson NATURE 139, 627 (1937).

Nature, 1938, 141, 247

10 AM Aug. 19. 57
92. Blood sugar .22
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sugar at this sample .22

SCHWANGERSCHAFTSDIAGNOSE AUS DEM HARN (DURCH HORMONANALYSE).
Von
S. ASCHHEIM und BERNHARD ZONDEK.
Von der Universität-Erkrankungsklinik der Charité in Berlin.
In dieser Wochenschrift 1927, Nr. 25, haben wir berichtet, daß im Harn der Schwangeren das beschriebene Sexualhormon

Pregnancy test. Klin. Wschr., 1928, 7, 8

Testosterone, 1935

Zeitschrift für angewandte Chemie

14. Jahrgang, S. 905-916. Inhaltsverzeichnis: Siehe Anzeigenblatt S. 258. 14. November 1931, Nr. 46

Über die chemische Untersuchung der Sexualhormone.

Von Prof. Dr. Dr. A. BUTENANDT.

Allgemeines Chemisches Universitäts-Laboratorium in Göttingen.

Vortrag auf der Tagung der Nordwestdeutschen Chemiker in Hamburg am 25. Oktober 1931.

Die biologische Forschung hat uns in den letzten Jahren, zur Lösung einer solchen Aufgabe, ein

Banting's notes on insulin, 1921

Isolation of androsterone by Butenandt, 1931

FEEDING EXPERIMENTS ILLUSTRATING THE IMPORTANCE OF ACCESSORY FACTORS IN NORMAL DIETARIES. BY F. GOWLAND HOPKINS.

(From the Physiological Laboratory, Cambridge.)

THE experiments described in this paper confirm the work of others in showing that animals cannot grow when fed upon so-called "synthetic" dietaries consisting of mixtures of pure proteins, fats, carbohydrates, and salts. But they show further that a substance or substances present in normal foodstuffs (e.g. milk) can, when added to the dietary in astonishingly small amount, secure the utilization for growth of the protein and energy contained in such artificial mixtures.

J. Physiol., 1912, 44, 425

Die Vitamine

ihre Bedeutung für die Physiologie und Pathologie

mit besonderer Berücksichtigung der

Avitaminosen:

(Beriberi, Skorbut, Pellagra, Rachitis)

Word "vitamine" introduced by Casimir Funk, 1914

Vitamin B₁ (aneurin), 1926

Vitamin C (ascorbic acid), 1928

Carotene (provitamin A), 1929

Vitamin D₂ (calciferol), 1931

Riboflavin, 1932

Biotin, 1936

α -Tocopherol allophanate crystals
Vitamin E, 1936

Vitamin B₆ (pyridoxin), 1938

J. Amer. med. Ass., 1926, 87, 470

TREATMENT OF PERNICIOUS ANEMIA BY A SPECIAL DIET*

GEORGE R. MINOT, M.D.

AND

WILLIAM P. MURPHY, M.D.

BOSTON

This paper concerns the treatment in a series of forty-five cases of pernicious anemia in which the patients were given a special form of diet. While the problem of diet in the treatment of pernicious anemia is by no means new, in our opinion its possible importance has not heretofore been generally recognized. In 1863, seven years after the publication of Addison's second, but best known, description of the disease now called pernicious anemia, Habershon¹ wrote concerning this condition: "Many patients at an early stage come under the influence of bracing air and stimulating diet." Other early writers, as Biermer² in 1872, argued the desirability of a form of medicine placed on the value that "cases well with all ordinary

* This study was supported by the Fund of the Harvard Medical School, the Hospital, and the Medical Service of the Harvard University Hospital. J. Habershon, S. (May 9) 1863.
2. Biermer: *Halt Zungen*, ... über eine von ihm älteste beobachtete eigenständige Form von progressiver perniciouser Anämie, welche mit Capillaren Blutungen der Haut, Retina, des Gehirns &c., ...

Vitamin B₁₂, 1948

Nicotinic Acid, 1937

Menaphthone crystals
Vitamin K, 1939

Million-volt apparatus installed in 1936 in St. Bartholomew's Hospital, showing the treatment room. Positive pole shown top right.

Ten-gramme radium unit installed in the Westminster Hospital, 1948; uranium has replaced tungsten as the protective metal.

Positive pole

Four-gramme radium bomb, 1933, Westminster Hospital

Thirty-million-volt synchrotron designed for the Medical Research Council and installed in the Physics Department, Royal Cancer Hospital, London, 1949.

Radiograph of foreign body in thumb, University College Hospital, 1896. Probably first diagnostic radiograph in Britain. Röntgen discovered *X* rays in 1895.

"Röntgen Rays" on active service, 1899

High-tension apparatus for producing *X* rays, 1900

"Skiagraphy in Urinary Surgery," 1906

Coil set and mercury interrupter, 1910

X-ray diagnostic unit, University College Hospital, 1949

Oxygen inhalation apparatus, 1903

"Perspex" oxygen tent, 1949

Zur Kenntnis der anti-fermentativen, lytischen und agglutinierenden Wirkungen des Blutserums und der Lymphe.
[Aus dem pathol.-anat. Univ.-Institute des Prof. Weichselbaum in Wien.]

Von Dr. Karl Landsteiner in Wien.

I. Zur Serumdiagnostik der Fermente.

Durch die Arbeiten von Ferri¹⁾, Pernossi²⁾, Hammarsten³⁾, Hahn⁴⁾, Röden⁵⁾, Hildebrandt⁶⁾ und Morgenroth⁷⁾ wurde festgestellt, daß dem Blutserum die Fähigkeit zukomme, die Wirkung mancher Fermente aufzuheben. Ferri und Hahn führten ihre Untersuchungen an verdauenden Fermenten aus, Röden und Morgenroth am Labenzym.

Discovery of blood groups, 1900; *Zbl. Bakt.*, 27, 357

An Agglutinable Factor in Human Blood Recognized by Immune Sera for Rhesus Blood

KARL LANDSTEINER AND ALEXANDER S. WIENER.

From the Rockefeller Institute for Medical Research and the Office of the Chief Medical Examiner of New York City.

The capacity possessed by some rabbit immune sera produced with blood of Rhesus monkeys, of reacting with human bloods that contain the agglutininogen M has been reported previously.^{1,2} Subsequently it has been found that another individual property of human blood (which may be designated as Rh) can be detected by certain of these sera.

Discovery of Rh factor, 1940; *Proc. Soc. exp. Biol. N.Y.*, 43, 223

Routine blood grouping with stock typing sera of groups A and B

Paraffin-lined transfusion tube used by Kimpton and Brown, 1913; *J. Amer. med. Ass.*, 61, 117 First transfusion of citrated blood, 1914; *An. Inst. mod. Clin. Méd.*, B. Aires, 1, 25

Spin-freezing plasma

Blood transfusion to-day

Die experimentelle Chemotherapie der Spirillosen

(Syphilis, Rückfallfieber, Hühnerspirillose, Framboesie)

Von

Paul Ehrlich und S. Hata

Mit Beiträgen von
H. J. Nichols, New York, J. Iversen, St. Petersburg, Bitter-Kairo
und Dreyer-Kairo

"606," Salvarsan, 1910

Sulphanilamide,
November, 1935

Prontosil, described by Domagk, 1935;
Dtsch. med. Wschr., 61, 250

250

DEUTSCHE MEDIZINISCHE WOCHENSCHRIFT

Aus den Forschungslaboratorien der I. G. Farbenindustrie A. G. Werk L.

Ein Beitrag zur Chemotherapie der bakteriellen Infektion.

Von Prof. GERHARD DOMAGK

Bisher war man im allgemeinen der Ansicht, daß nur Protozoeninfektionen chemotherapeutisch angreifbar wären. Auf dem Gebiet der Protozoeninfektionen besitzt man kausal wirksame Arzneistoffe, z. B. gegen die Trypanosomien-

Mäuseversuch eine Andeutung von Wirkung bei der Streptokokkensepsis erkennen ließen. Wir hatten unter den Azokindinverbindungen eine Reihe von Substanzen kennen gelernt, die eine relativ gute Wirkung im in vitro-Desinfek-

ON THE ANTIBACTERIAL ACTION OF CULTURES OF A PENICILLIUM. WITH SPECIAL REFERENCE TO THEIR USE IN THE ISOLATION OF *B. INFLUENZÆ*.

ALEXANDER FLEMING, F.R.C.S.

From the Laboratories of the Inoculation Department, St Mary's Hospital, London.

Received for publication May 10th, 1929.

with staphylococcus variants a number of plates were necessarily exposed to the action of various micro-organisms

British Journal of
Experimental Pathology,
1929, 10, 226

Fleming's original plate, 1929

Penicillin G, 1943

Streptomycin, 1944

Chloromycetin, 1947

Aureomycin, 1948

Self-recording control panel used in preparation of antibiotics

Penicillin deep-culture vessels

Filling vials with streptomycin

Electronically controlled freeze-drying plant for low-temperature dehydration of yellow-fever vaccine

The "new" General Hospital, Birmingham, in Steelhouse Lane, opened in 1897

The Queen Elizabeth Hospital and the Medical School of the University of Birmingham, which were opened in 1938

In the absence of mortality statistics derived from death certificates a review of 50 years' progress would of necessity have consisted of one great question mark. Given the full co-operation of the medical profession in the difficult and

somewhat thankless task of writing down causes of death "to the best of my knowledge and belief," a review of progress 50 years hence will tell the story in much more illuminating fashion than has been possible to-day.

MEDICAL PROGRESS FROM 1850 TO 1900

BY

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The preceding articles survey the progress of medicine from 1900 to 1950. So that the reader may see this in perspective Professor Singer here traces the development of medical ideas in the fifty years before 1900.

History does not really accommodate itself to those exact dates and places that we learned at school. The Norman Conquest did not begin and was not ended at Hastings on October 14, 1066. The struggle extended over a far wider area, started generations before, and was not completed till long after—if it ever was completed. And so with the history of medicine. It is a deceptive anecdotal simplification to write it as though it consisted of a series of great discoveries each made by a particular investigator in a named year. Knowledge seldom advances by such precise and measured steps. Were I to follow that method here, this little essay would be a mere list of names and dates, and misleading ones at that.

It must be remembered, too, that discoverers no more work by themselves than do other men. Each is necessarily a member of a society—a community of men much like himself. Even the most austere and secluded man of science must have some audience in his mind—why else should he publish his results? He derives knowledge and ideas from his predecessors. He discusses his work with his colleagues. They criticize it. For some of his data he must depend on his co-workers and assistants and even on his opponents. Movements are greater than men; let us then follow them rather than the mere sons of Time. I have, for once, excluded all names from my narrative. The reader will doubtless supply them for himself.

The intellectual motives which lay at the root of medicine between 1850 and 1900 differed very considerably from those of the following half-century. To one who would contrast them with as little trouble and as much pleasure as he may, I would say: "Read two magnificent novels dating from the middle of the two periods, *Middlemarch* (1872), by George Eliot, and *Martin Arrowsmith* (1925), by Sinclair Lewis." A comparison of the characters and careers of the medical heroes in these two masterpieces, Lydgate and Arrowsmith, will go far to attaining the purpose of this number of the *British Medical Journal*.

In the decade around 1900, with which I must end my story, there were several highly significant redirections of medical thought. I am not now concerned with these. My task is rather to indicate how there arose the intellectual and scientific situation which determined them. It will be a generation before anyone will be able to say with assurance whether this year of 1950 and its surrounding years can also be regarded as a critical period for the history of medical science—for medicine is now indeed a science, which it was not in 1850. But to make history intelligible we must somehow divide it into periods. It is, then, truly the case that the years around 1900 provide a favourable and convenient opportunity for beginning to take stock of the state of medicine now. 1900 or a decade or two earlier is, moreover, about as far back as the scientific memory of living individuals usefully extends. On the other hand, 1850 is not a very tractable beginning, and I

wish that I could have chosen another year for that purpose. In considering nineteenth-century medicine it must be remembered that the British medical schools have a peculiar history that differs fundamentally from that of the Continental schools. The British schools were later in coming into being. They arose actually, or by imitation, or by tradition, from a system of apprenticeship. The Royal Colleges in Britain, which came largely to control medical practice in the nineteenth century, were formed with the ancient Guild Companies of Craftsmen and Merchants in mind. An actual apprenticeship was once part of the normal career of a medical practitioner. The influence of the universities on medical thought and on medical education in Britain was trifling. It was also slightly artificial, except at Edinburgh. The great majority of students and a large proportion of teachers took only the examinations of the Colleges. The teachers in each school formed a close corporation. On the Continent, on the other hand, it was the medical faculties of the universities that were the effective agents of medical education. They too were the natural centres for scientific and medical research. Continental universities were under governmental control and had governmental financial support, conditions then quite unknown in this country. In nineteenth-century England the only branch of medicine that was the object of attention from the State was that known as "preventive." Towards the very end of the period tropical medicine also aroused some official interest.

Administrative Interest in Medicine

The great Public Health Act and the Nuisances Removal and Diseases Prevention Act were passed in 1848. They came to be operated by a new Government department, the General Board of Health. The work of this Board was taken over, for administrative and political reasons, by the Privy Council. The Medical Department of the Council became part of the Local Government Board (1871), the functions of which were, in the twentieth century (1919), absorbed by the new Ministry of Health.

Just as the General Board of Health came into action there was an outbreak of cholera in England, of which some 54,000 persons died. Statistics available under the new system made possible the deduction that the infection was conveyed by drinking-water. This led to suitable precautions. It is one of the many instances in which preventive practice preceded any knowledge of the organic cause of a disease, or indeed any direct knowledge of disease germs at all. Unfortunately, such successes—which were not a few—were often misinterpreted in such a way as to encourage faith in an attitude wrongly described as "practical." With this vague and foolish word ignorant men have comforted themselves for centuries. With it they have sought to conceal from themselves and from others their destitution of anything in the nature of general