administered by exceptional men practically renders negative the evils of the Malthusian theory.

1. The greater the population the greater the number of exceptional men of all degrees, since exceptionality depends on a ratio to the total population.

2. The value of the work of a given exceptional man capable of producing an invention, depends on the value of the invention to the average man who uses it, multiplied by the number of users, who are in ratio to the total population.

3. Two results emerge: (a) The value of the work of an exceptional man increases directly with the growth of the population. (b) Society gains greatly through the increase in its numbers, since every member of the population on the average is served by all of the exceptional men. The value of the work of a Luther Burbank, an Edison or an Eli Whitney is incalculable.

From the standpoint of eugenics, it is desirable: (1) To select as early as possible the exceptional minds; (2) to afford these minds every opportunity of training and education; (3) to place them in operation where their exceptionality may prove advantageous to society; (4) to place in operation instantaneously the results of their work. How large are the appropriations now made for the defective children who must forever be a burden on society. How little has been done for the exceptional children who must carry by their work both the defective and the average of the population. Professional organizers understand the importance of this phase, Carnegie in his libraries and institutes, Rockefeller in the Rockefeller Institute and Chicago University. *A fortiori* the nation should provide for this necessity.

The economic reasons for establishing a National Department of Health are five:

1. To enable society to progress more rapidly under the law of increasing returns through increasing the percentage of exceptional men of each degree (many of whom are now lost through preventable accidents), in addition to increasing the total population.

2. To lessen the burden of the unproductive years on the productive years by increasing the average age at death. If we estimate the average span at 40 years, and 20 years as unproductive, the ratio of unproductive to productive years is 100 per cent. Without venturing an opinion as to the true figures after the manner of La Place, I have calculated what would be the economic gain if average span were 40, 45, 50 and 55 years and also the burden of an unproductive year at \$100 and \$200. The annual gains are shown under the various hypotheses. Thus if the average life-span of a class of the population can be increased from 40 to 45 years, the economic gain would be \$25 to \$50 per head. Assuming 40,000,000 of productive age in the United States, the burden of the unproductive years of childhood, lightened by an increase in the average life span, from 40 to 45 years would be \$800,000,000 to \$1,600,000,000 per annum, and an increase of ten years would result in savings of \$1,320,000,000 to \$2,640,000,000 per annum.

BURDEN OF UNPRODUCTIVE YEARS ON PRODUCTIVE YEARS.

Average span of life in years	40	45	50	55
At \$100, per cent	100	80	67	57
Measured in dollars, per capita	\$100	\$ 80	\$ 67	\$ 57
Gain for period		20	13	10
Total gain		20	33	43
At \$200	200	160	134	114
Gain for period		40	26	20
Total gain		40	66	86

3. The third economic reason for establishing a de-

partment of health is to decrease the burden of death on the productive years by increasing the age at death. If the expense of illness and death are \$300, and the average age at death is 40 years, the average death expenses average \$15 on the twenty productive years. Could the average age be increased to 50 years, the burden falls to \$10, or a decrease of 50 per cent. For 80,000,000 of people, the saving of \$1.50 per year of life would be equivalent to \$120,000,000 per annum.

4. The fourth object of the plan would be to lessen the economic burden of sickness. Assuming Newholme's figure of 9 days' average illness per annum, approximately 2,000,000 years of life are lost per annum. Estimating wages at \$1 a day, and all other expenses \$1 a day, \$1,444,000,000 loss per annum is registered by this item. Could the days of illness be cut down one-third, nearly \$500,000,000 would be saved.

5. Higgins has estimated that six hundred millions are now spent on criminality in the United States. If the criminality is largely the product of the social environment, such as overcrowding, alcoholism, etc., measures which would decrease this only fractionally are worthy of consideration. A decrease of 16 2/3 per cent. would result in savings of \$100,000,000 per annum.

For the last four estimates the total savings range between \$1,800,000,000 and \$4,000,000,000 per annum.

In addition to the economic gain, the establishment of a National Department of Health would gradually but surely diminish much of the misery and suffering that can not be measured by statistics. Sickness is a radiating center of anxiety; and often death in the prime of life closes the gates of happiness on more than one life. Let us not forget that the "bitter cry of the children" still goes up to Heaven and that civilization must hear, until at last it heeds, the imprecations of forever wasted years of millions of lives.

If progress is to be real and lasting, it must provide whatever bulwarks it can against death, sickness, misery and ignorance; and in an organization such as a National Department of Health—adequately equipped—a vast preventive machine—working ceaselessly, an attempt at least would be made to staunch those prodigal wastes of an old, yet wastrel world.

HYPERSENSITIBILITY.*

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(Abstract.)

The phenomenon of hypersusceptibility has long been recognized, but has been overshadowed in modern studies on immunity. Instances of hypersusceptibility to certain infectious diseases, bacterial toxins and other substances may be found scattered through the literature. The well-known hypersusceptibility to tuberculin in animals infected with tuberculosis has received much attention, but the importance of hypersusceptibility in general pathology has not been realized.

At first glance it would appear much more important for an organism to be *hyposensitive* than *hypersensitive* to infectious processes, but a closer study of the com-

* Read in the Section on Pathology and Physiology of the American Medical Association, at the Fifty-seventh Annual Session, June, 1906.

plex problems of immunity develops the curious fact that resistance to disease may be largely gained through a process of hypersusceptibility. Whether this increased susceptibility is an essential element or only one stage in the process of resistance to disease must now engage our attention.

Von Pirquet and Schick¹ believe the immunity which an organism acquires after an attack of measles, whooping cough, etc., consists in the power of "immediate reaction;" that is, a condition of hypersensitiveness. This immediate reaction is an expression of cellular resistance rather than humeral or antitoxic immunity.

Our studies² on the hypersusceptibility produced in guinea-pigs by the injection of horse serum have a direct bearing on this question. We have shown that these animals may be rendered acutely sensitive to a substance which is incapable in itself of producing apparent harm.

HYPERSENSITIBILITY TO HORSE SERUM.

It has long been known that the blood of certain animals is poisonous when transfused or injected into certain other species. Many instances might be cited showing that the blood serum of one animal has poisonous properties when injected into an animal of another species. But the blood serum of the horse apparently lacks such poisonous action. Very large quantities of the blood serum of the horse may be injected into man, rabbits, guinea-pigs, and many other animals without serious inconvenience, except occasionally a slight reaction at the site of inoculation. In a certain proportion of cases the injection of horse serum into man is followed by urticarial eruptions, joint pains, fever, swelling of the lymph nodes, edema, and albuminuria. This reaction, which appears after an incubation period of 8 to 13 days, has been termed by Pirquet and Schick the "serum disease." In exceptional instances sudden death has followed an injection of horse serum in man.

These studies were taken up in October, 1905, by one of us (Anderson), in order to throw light on the cause of this unfortunate accident. We have shown that ordinarily horse serum is a comparatively bland and harmless substance when injected into certain animals; but these animals may be rendered so susceptible that an injection of horse serum may produce sudden death or severe symptoms. For example, large quantities of horse serum may be injected subcutaneously or into the peritoneal cavity of a guinea-pig without apparently causing the animal the least inconvenience. But if a guinea-pig is injected with a small quantity, say .004 c.c., of horse serum and after the expiration of a certain interval is again injected with horse serum the result is usually fatal. The first injection of horse serum has sensitized the animal in such a way as to render it very susceptible to a toxic principle in horse serum. It is probable that when the guinea-pig is injected with the first, or sensitizing quantity of serum the strange proteid contained in the horse serum develops in the body of the guinea-pig "antibodies" which, when brought into contact with more horse serum given at a second injection, produce either a union or reaction, which causes the toxic action. A certain time must elapse between the first and second injections of horse serum before this toxic action is able

to manifest itself. This "period of incubation" is from ten to twelve days, and corresponds suggestively with the period of incubation of the serum disease which Pirquet and Schick place at eight to thirteen days.

Guinea-pigs may be sensitized with exceedingly small quantities of horse serum. In most of our work we used quantities less than .004 c.c. and we found in one instance that .000,001 c.c. of horse serum was sufficient to render a guinea-pig susceptible. It also requires very small quantities of horse serum, when given in a second injection, to produce poisonous symptoms. The injection of 1 c.c. into the peritoneal cavity is sufficient to cause the death of a half-grown guinea-pig. The injection of .1 c.c. of horse serum subcutaneously is sufficient to produce serious symptoms. The fact that this toxic action may be developed by such small quantities of serum and the fact that exceedingly small quantities are sufficient to produce symptoms and death on a second injection, and the further fact that an immunity may be produced against this toxic action, *a priori*, places both the sensitizing and the toxic principle in the horse serum in the "hatpin group" of substances in the sense used by Ehrlich.

While at first we thought that diphtheria antitoxin had some relation to this action, we are now able to state positively that it has nothing whatever to do with the poisonous action of horse serum; further, that diphtheria antitoxin in itself is absolutely harmless. The toxic action which we have studied is caused by a principle in normal horse serum and is entirely independent of the antitoxic properties of the serum.

The chemical and vital processes of the body must be delicately balanced when we consider that the introduction into the system of a small quantity of horse serum is sufficient to break the compensation in such a way that the subsequent injection of the same substance is capable of producing sudden and serious symptoms. This remarkable phenomenon must increase our wonder of the manifold and mysterious vital phenomena which constitute life, and accentuate our ignorance of many of its fundamental processes.

An active immunity against this toxic principle may readily be established by repeated injections of horse serum, at short intervals, into a guinea-pig. Although guinea-pigs may be immunized actively in this manner, we have not yet succeeded in transferring this immunity in the blood serum or body juices to another guinea-pig. It, therefore, appears that the immune bodies, if such exist against the toxic action of horse serum, are not free in the blood and body juices contrary to the case in diphtheria.

Guinea-pigs may be sensitized to the toxic action of horse serum by feeding them with horse serum or horse meat. The fact that guinea-pigs may be rendered susceptible by the feeding of strange proteid matter opens an interesting question as to whether sensitive guinea-pigs may also be poisoned by feeding with the same serum given after a proper interval of time. If man can be sensitized in a similar way by the eating of certain proteid substances may not this throw light on those interesting and obscure cases in which the eating of fish, sea food and other articles of diet habitually causes sudden and sometimes serious symptoms?

The susceptibility to the toxic action of horse serum is transmitted from the mother guinea-pig to her young. These results on the hereditary transmission of the susceptibility to the poisonous action of horse serum in

1. Von Pirquet, C. F., and Schick, B.: Die Serumkrankheit, Leipzig, 1905, p. 144.

2. Rosenau, M. J., and Anderson, John F.: "A Study of the Cause of Sudden Death Following the Injection of Horse Serum," Bulletin 29, Hygienic Laboratory, U. S. Public Health and Marine-Hospital Service, Washington, April, 1906, p. 95.

guinea-pigs may throw light on the well-known hereditary tendency to tuberculosis in children born of a tuberculous parent. There are certain analogies between the action of tuberculosis and horse serum. Both may produce a hyper-susceptibility and also a certain degree of immunity. Now that we have proved this hypersusceptibility or anaphylactic action in the case of horse serum may be transmitted hereditarily in guinea-pigs, may it not throw light on the fact that tuberculosis "runs in families?"

Demonstrations of the hereditary transmission of acquired characters are comparatively rare in biology. While there are several recorded instances demonstrating that immunity to certain infectious diseases may be transmitted from a mother to her young, yet, as far as we know, this is the first recorded instance in which hypersensitiveness, or anaphylaxis, has been experimentally shown to be transmitted from a mother to her young.

It may be that man can not be sensitized in the same way that we have shown to be the case with guinea-pigs. In a number of instances children have been injected with antidiphtheric horse serum at short and long intervals without, so far as we are aware, causing death. Certain serums, for example, the antitubercle serum of Maragliano and the antirheumatic serum of Menzer, are habitually used by giving injections at intervals of days or weeks. In all such cases of frequent and repeated injections the amount which has been injected and the interval between the injections must be taken into account in relation to our work. Von Pirquet and Schick have shown that a second injection of horse serum into children causes an "immediate" or an "accelerated" reaction. Both the immediate and the accelerated reaction in children are characterized by symptoms of the "serum disease."

We might conclude that children may not be sensitized to the toxic action of horse serum by eating horse meat, for horse meat is a favorite article of diet in certain European countries and there is nothing on record to show that the injection of horse serum in those countries is fraught with more danger than where this diet is not used. It should be borne in mind that our work has shown that guinea-pigs may be sensitized with exceedingly minute quantities of a strange proteid, and that repeated injections cause an immunity, and it does not seem impossible that the same action may be true of food.

Man reacts to the first injection of horse serum after a period of 8 to 13 days; guinea-pigs show no reaction as a result of the first injection; both man and guinea-pigs react to a second injection. The reactions in man and the guinea-pig differ both in severity and in kind. The relation, therefore, that our observations on the guinea-pig may have in their application to man must await further study. The fact that other animals beside man and the guinea-pig react to a second injection of horse serum would seem to indicate that we are dealing with one and the same action.

We believe that our results make it probable that man may be rendered sensitive to the injection of a strange proteid, as is the case with the guinea-pig and other animals, and that this explanation must be considered as well as the *status lymphaticus*, which has heretofore been assigned as the cause of sudden death following the injection of horse serum.

Our studies do not detract from the great usefulness of diphtheria antitoxin. This sovereign remedy, when

used early in the disease, decreases the death rate to almost *nil*. We can not be blind to certain inconveniences and occasional dangers in the introduction of horse serum into the system, but the benefits far outweigh the dangers. In view of these facts we are now engaged in refining diphtheria antitoxin in an attempt to eliminate this undesirable principle present in the horse serum.

DISCUSSION.

DR. V. C. VAUGHAN, Ann Arbor, Mich., said that for a number of years he had been at work at poisons from bacterial cells, albumin, peptones, etc. Dr. Rosenau showed him some of his guinea-pigs inoculated with the second horse serum. They die almost exactly as Dr. Vaughan's guinea-pigs die with the isolated poison, but there is apparently this difference: With isolated poisons there is a rapid fall in temperature, and Dr. Rosenau made an experiment on one guinea-pig which practically died at the time, and there was no fall in the temperature. Every protein molecule has a poisonous group. With all the proteids he has worked with, this poisonous substance was found and has a benzene ring in it, gives the Millon test and, on being broken up with strong acids, characteristic reactions followed. This substance is a chemical nucleus of the molecule. He believes that life is molecular and that in the living cell the side-chains are the receptors. They are the side-chains which feed and break up the pabulum which comes in contact with the living cell. Oxygen is taken on and this is converted into CO₂. This is the normal metabolism. The relative distances between the atoms in the molecule are as great as the distances between the planets of the solar system. When one group gets over into range with another group and combines with it, it forms water and carbonic acid gas. That is the normal way in which the cell functionates. There is no other possible explanation of the way in which a cell feeds. By heating albumin, bacterial cells, etc., the proteid molecule is split up from the food receptors. That is the center of chemism. Dr. Vaughan thought that if Dr. Rosenau will take these proteids in the blood serum and heat them there is no doubt that he will split off this body. It is very stable. Dr. Vaughan has kept solutions for two years. They have decreased in toxicity. There is no carbohydrate in the chemical nucleus of the molecule. That is, in the side-chains which are split off. It is readily soluble in alcohol. He would call it albuminose, which is different from the ordinary albuminoses. The Rosenau-Anderson phenomenon may be explained on the ground that when you first inject the horse serum the cells of the guinea-pig split up the proteid molecule. Why doesn't the first injection kill? Because the cells of the animal body split up this substance slowly. The same is true of the isolated poison, as has been demonstrated time and time again by using many times the fatal dose. If you will take a rabbit and make him fast several days, then fill his stomach two or three times with the fatal dose, it will not kill. The poison is diffused. Now when he injects his horse serum the first time the cells of the guinea-pig decompose that proteid molecule, but so slowly that the poison which is set free has no appreciable effect on the animal. If he makes his injections every day he establishes a tolerance for the poison, so that after ten days he can inject without any effect, but when he waits ten days the cells tear the molecule to pieces quicker than before, this sets the poisons free quicker and the animal dies. Dr. Vaughan said that this is his present idea. It may be altogether wrong, but there is a wonderful field here for research. He is very certain that the phenomenon has a very direct relation to the work he has been doing, because the symptoms which he has produced are the same, unless it be on the point of temperature. He is sure Dr. Rosenau will find that when he isolates this substance it will resist up to 100 degrees. It will not do it as long as it is in the proteid molecule. The results come from the tearing off of side-chains from body cells, side-chains the functioning of which is necessary for the maintenance of life, and if one injects it directly into the blood it will kill in a few seconds or minutes, and if in the peritoneal cavity in a half-hour or so. He hoped more would take up this work.

Dr. G. F. RUEDIGER, Chicago, said that about a year ago he was approached on this subject of untoward symptoms following the use of antitoxin by the representative of a manufacturer of antitoxin, who showed letters indicating that the writers got their most serious results after several injections had been given. From the reports in the literature he came to the same conclusion mentioned by Dr. Rosenau: that is, that many of the most alarming symptoms are observed after the first injection. The letters showed, however, that these doctors got very alarming symptoms, with collapse in some instances, after several injections had been given and not after the first injection. These reports are not published, as a rule.

Dr. THEOBALD SMITH, Boston, said the subject had interested him since 1902, although no special effort has been made to analyze the phenomenon. He remarked that guinea-pigs which have received no preliminary doses of serum may die and that of those which have received a fairly large dose of serum at the outset nearly all are thereafter immune. The problem, therefore, is very complicated. He presented his results in the following table:

GUINEA PIGS

Preliminary treatment	Final treatment	Number treated	RESULTS			% of illness or death
			Died	Re-covered	No effect	
3cc-5cc diph. antitoxin	3-5cc diph. antitoxin	31	2	—	29	6.45
nothing	3-5cc diph. antitoxin	58	9	—	49	15.5
diphtheria toxin only	3-5cc diph. antitoxin	10	—	—	10	0
diph. toxin + antitoxin (serum 1/200-1/400cc)	3-5cc diph. ant toxin	18	10	3	5	72.3

Dr. Smith said that an interval of two or three minutes elapsed between the first and second injections. None died after the first treatment. He did not know whether or not the animals were the young of guinea-pigs that had been treated.

Dr. ROSENAU said that he wished that he could believe that Dr. Vaughan's explanation is the correct one, being so plain and succinct. It is very easy to expand Ehrlich's side-chain theory to fit these facts by adding, subtracting or modifying a receptor. Dr. Anderson and he had felt that they could safely let Ehrlich modify his own theory to include the new facts. With Dr. Vaughan he realized that chemistry may some day explain the complex and multiple processes constantly going on in living protoplasm. It seemed to him that science has not yet reached that stage where it can assign a definite chemical molecular structure to such a complex, highly-organized and changing substance as protoplasm. Those who constantly deal with the material sciences would like a physical or chemical explanation of life. A correct explanation of the phenomenon studied in the guinea-pig would bring nearer the solution of many problems connected with metabolism and the fundamental processes on which existence depends.

DETERMINATION OF THE NORMAL TEMPERATURE OF THE CLOSED INGUINAL FOLD OF A CHILD, AND ITS CLINICAL SIGNIFICANCE.*

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CHICAGO.

HISTORY.

The practitioner of medicine is constantly looking to science and research for methods he may use in his routine work. Most practitioners seek methods which combine two characteristics, accuracy and practicability,

but these are often diametrically opposed. I have attempted to solve a problem in a manner that shall yield results at the same time accurate and easy of application to the clinical case.

Normal and pathologic conditions in the animal body are very intimately connected with, and in fact dependent on, the production, the distribution and the variation of that phenomenon called animal heat.

Medical and scientific literature is replete with all phases of this subject, and I intend to touch on only those points of measurement which may be included in the term thermometry.

The practitioner usually adopts the practice of taking the patient's temperature as one of the first steps in his routine examination. Two methods of estimation as pertains to clinical thermometry are in vogue, namely, the internal and the external. Both have their adherents and applications. Some writers contend that the only true measurement of the temperature of the body can be obtained from the internal cavities, while others state that external methods are sufficiently correct for purposes of clinical study.

The following table shows the results of observations by several authors who have made extended studies along these lines:

TABLE 1.

Maximum.		Minimum.		Mean.		Author and Place.
F.	C.	F.	C.	F.	C.	
99.05	37.2	97.7	36.5	98.42	36.9	Davy ¹ : Mouth.
99.5	37.5	98.24	36.8	99.05	37.2	Gierse ² : Mouth.
98.6	37.0	97.34	36.3	98.06	36.7	Hooper ³ : Mouth.
99.14	37.3	97.88	36.6	98.6	36.7	Hallmann ⁴ : Mouth.
98.6	37.0	97.88	36.3	98.24	36.8	Clifford Allbutt ⁵ : Mouth.
100.4	38.	97.16	36.2	98.6	37.0	Wunderlich ⁶ : Axilla.
99.32	37.4	96.98	36.1	98.24	36.8	Leibermeister ⁷ : Axilla.
98.78	37.1	98.06	36.7	98.42	36.9	Damrosch ⁸ : Axilla.
99.32	37.4	96.98	36.1	98.06	36.7	Billet ⁹ : Axilla.
100.2	37.9	97.34	36.3	98.78	37.1	Billroth ¹⁰ : Axilla.
100.4	37.8	97.7	36.5	99.05	37.2	Turgenson ¹¹ : Rectum.
98.78	37.1	97.88	36.6	98.24	36.8	Neubaus ¹² : Rectum.
99.14	37.3	98.42	36.9	98.78	37.1	Jaeger ¹³ : Rectum.
99.32	37.4	96.98	36.1	98.24	36.8	Nicol ¹⁴ : Rectum.
99.5	37.5	99.32	37.4	99.14	37.3	Hall ¹⁵ : Rectum.

The average of the mean observations in Table 1 for the mouth temperature is 98.47 F. (36.93 C.), for the axilla 98.43 F. (36.91 C.), for the temperature of the rectum 98.81 F. (37.12 C.). This shows that the difference between the mouth temperature and the axillary temperature is very small, approximately .04 F. (.02 C.). The variation between the axillary and rectal temperature is somewhat larger, being .38 F. (.21 C.). The maximum average for the temperature of the mouth is 99.42 F. (36.91 C.), the minimum being 98.47 F. (36.93 C.); for the axilla, maximum 99.60 F. (37.56 C.), minimum 98.42 F. (36.91 C.), and for the rectum,

1. Davy: Phil. Trans., London, 1845, part 2, p. 319.
2. Gierse: "Quænam sit ratio caloris organici, etc." Halae, 1842, p. 40.
3. Hooper: Med. Times and Gaz., London, 1866, vol. ii, p. 483.
4. Hallmann: Quoted from Landolt's Lehrbuch d. Physiol. Aufg. 3, S. 406.
5. Clifford Allbutt: Jour. Anat. and Physiol., London, 1872, vol. iii, p. 106.
6. Wunderlich: Medical Thermometry, p. 95.
7. Leibermeister: "Handbuch d. Path. u. Therap. d. Fleberd," 1875, p. 78.
8. Damrosch: Deuts. Klinik, Berlin, 1862, vol. ii, p. 331.
9. Billet: These, Strasburg, 1869.
10. Billroth: Arch. f. Klin. Chir., Berlin, 1862, vol. ii, p. 331.
11. Turgenson: "Die Körper warme des gesunden Menschen," Leipzig, 1873.
12. Neubaus: Virchow's Arch., 1893, vol. cxxiv, p. 365.
13. Jaeger: Deuts. arch. f. klin. Med., Leipzig, 1881.
14. Nicol: Quoted.
15. Hall: "Text-Book of Physiology."

* Read in the Section on Pathology and Physiology of the American Medical Association, at the Fifty-seventh Annual Session, June, 1906.

* From the Department of Physiology, Northwestern University Medical School.