NON-SPECIFIC PROTEIN THERAPY
IN SYDENHAM'S CHOREA

BY

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<table>
<thead>
<tr>
<th>INDEX</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>1</td>
</tr>
<tr>
<td>Pathology</td>
<td>3</td>
</tr>
<tr>
<td>Anatomico-pathological findings and their physiological correlation</td>
<td>4</td>
</tr>
<tr>
<td>Therapeutic measures</td>
<td>6</td>
</tr>
<tr>
<td>Non-specific protein therapy</td>
<td>10</td>
</tr>
<tr>
<td>The reaction after the intravenous injection of a vaccine</td>
<td>12</td>
</tr>
<tr>
<td>Application in chorea</td>
<td>19</td>
</tr>
<tr>
<td>The method used in the present series of 25 cases</td>
<td>25</td>
</tr>
<tr>
<td>Mode of administration</td>
<td>26</td>
</tr>
<tr>
<td>The list of cases treated</td>
<td>28</td>
</tr>
<tr>
<td>Therapeutic results</td>
<td>88</td>
</tr>
<tr>
<td>Relapse rate</td>
<td>93</td>
</tr>
<tr>
<td>Discussion</td>
<td>94</td>
</tr>
<tr>
<td>Summary and conclusions</td>
<td>106</td>
</tr>
<tr>
<td>References</td>
<td>108</td>
</tr>
</tbody>
</table>
INTRODUCTION.

The treatment of Sydenham's chorea has always been empirical and symptomatic. Under a regimen of rest in bed, isolation, and the judicious administration of sedatives and hypnotics, the disease which is self-limiting, will usually run its course within 2 to 6 months, depending upon the severity of the attack and the resistance of the patient. Rest is the fundamental principle of treatment. Unfortunately, however, most cases are drawn from the poorer urban class, in whose homes it is more or less impossible to secure adequate rest. As a result, large numbers of cases of chorea have to be hospitalised for extensive periods at great expense to the community. It is but logical then, that any safe method of treatment, which promises to cure the condition more rapidly, is worthy of an extended clinical trial in both the private and the public weal.

On such a basis, non-specific protein therapy and, more recently, pyretotherapy produced by means of physical agencies would seem to merit closer investigation. The application of non-specific protein therapy to a series of 25 cases of Sydenham's chorea has been chosen as the subject of the present thesis. The treatment was undertaken during the writer's year of office as Resident Medical officer at the City General Hospital, Leicester. The results obtained are compared/
compared with those elicited in a control series of 25 cases treated by other methods.
The success of therapeutic endeavour is comparable with the knowledge of the pathogenesis of disease. The multiplicity of the remedies exhibited in Sydenham's chorea indicates our ignorance in this respect. In the same way, the profusion of explanations of the signs and symptoms of the condition is in inverse proportion to our actual understanding of the neurophysiology involved. A fundamental difficulty is of course that the anatomical basis of the disease is still uncertain, typical uncomplicated cases very rarely coming to autopsy.

PATHOLOGY.

Practically all recorded post-mortems have been carried out on cases with an associated rheumatic carditis, in which the possibility of the cerebral changes found being attributable to pyrexia and capillary embolism cannot be excluded. "The most common findings are scattered minute haemorrhages and capillary emboli, possibly most marked in the lenticular region of the basal ganglia. Very often the brain shows nothing, sometimes only hyperaemia. In some instances slight but diffuse encephalitic foci have been demonstrated. Marked thromboses have been described."

(Wechsler, 1935)

The association of encephalitic foci and meningitis in some cases has given rise to a widely-held belief that the essential change is a meningo-encephalitis.
There is considerable evidence that choreiform movements may follow lesions of the superior cerebellar peduncle, the corpus Luysii, the optic thalamus, the caudate nucleus, and the lenticular nucleus.

Bonhoeffer originally drew attention to the occurrence of chorea following lesions of the superior cerebellar peduncle ("Bindearm" chorea).

Kinnier Wilson (1928) regards chorea as a disorder of cortical function. He stresses the complex nature of the involuntary movements and also the fact that they are abolished on the affected side by a complete hemiplegia. He considers that some lesion or interruption in the pathways from the cerebellum to the motor cortex (via the superior cerebellar peduncle, red nucleus, hypothalamus, and thalamus) will cause a disorder of voluntary movement, together with involuntary movements produced by "a persistent (or intermittent) stream of disordered cerebello-cerebral afferent stimuli."

Martin (1927) holds the view that the condition is produced by a lesion of the corpus Luysii in the hypothalamus.

Most neurologists, however, believe in the striatal origin of chorea. The striatum is apparently a motor organ containing two types of cell--large and
and small - and connected with the thalamus and the cortex, the hypothalamus, the red nucleus, the substantia nigra, and the cerebellum. It apparently has an inhibitory influence on lower segmental reflex activity. Hunt (1917) is of the opinion that the large cells are associated with movement and the small cells with inhibition. Foerster (1921) considers that the function of the small cells may be co-ordinative and that of the large cells inhibitory of the activity of the pallidum. In chorea both postulate a lesion of the small cells only.

The more modern trend of opinion seems to be that it is essentially caused by an irritative lesion of the globus pallidus. There is thus an over-action of the pallidal fibres passing to the red nucleus and substantia nigra in the mid-brain, with a consequent over-exercising of the control held over the cerebellar fibres continued in the mids- spinal tract. This conception offers a plausible explanation of the muscular hypotonia and dyssynergia. On the same basis it can be argued that a diminution of the efferent cerebellar impulses passing to the anterior horn cells allows a more uncontrolled passage of motor impulses from the pyramidal pathways.

The supposed irritative pallidal lesion would, in most/
most cases of Sydenham's chorea, appear to be associated in some way with a rheumatic infection. Mental trauma is said to be a frequent exciting factor.

**THERAPEUTIC MEASURES.**

Remedies have been legion, and the routes of administration manifold, as the following list will show;

**ORAL:** Antirheumatic agents, such as sodium salicylate and aspirin; sedatives and hypnotics, such as, luminal, trional, chloral, paraldehyde, bromides and chloretone; phenazone; nirvanol; thyroid; parathyroid; calcium lactate; Fowler's solution; iodine; quinine; glycerophosphates; cod liver oil and other preparations containing vitamins A. & D.; yeast.

**SUBCUTANEOUS:** Adrenaline; sodium cacodylate; Rosenow's antiserum; tuberculin; varieties of antistreptococcal sera; hyoscine; morphia; pituitrin; distilled water.

**INTRAMUSCULAR:** Sulpharsenamine; Sodium evipan; magnesium sulphate; toxicotherapeutic agents (vide infra)

**INTRATHECAL:** Magnesium sulphate; colloidal silver; gentian violet; phenol 1% solution; atoxyl; sodium salicylate; streptococcal antisera; autoserum.
RECTAL: Avertin; paraaldehyde; sodium evipan.

VARIOUS MEASURES: Removal of septic foci, e.g. tonsils; ketogenic diet; hydrotherapy; psychotherapy; hypnosis; pyretotherapy by physical methods (vide infra).

Some of these methods will be discussed in greater detail.

NIRVANOL, or phenyl-ethyl-hydantoin, a near relation of the barbiturates, was first introduced as a hypnotic, but soon fell into disfavour because of its tendency to produce a skin eruption. It was introduced in Germany by Roeder (1919), who used it as a sedative in 2 cases of chorea with good results. Subsequently a host of confirmatory reports were published. In my own experience, it is a drug which definitely shortens the attack in a useful proportion of cases. However, it is effective only after toxic dosage, and consequently, although still widely used, it has gradually fallen into disfavour again, chiefly because a number of fatalities have been reported. Apart from these, dangerous side actions have been noted, such as serious leucopenia and thrombocytopenia, purpura, mucosal haemorrhages (Jones and Jacobs, 1932), and bloody diarrhoea; jaundice (Keller, 1928); severe lung complications (Piltz, 1927; Jones and Jacobs, 1932); renal damage (Pilcher and Gerstenberger, 1930). Many/
Many authors have observed relapses at varying intervals after primary successful treatment with nirvanol, but the relapse rate is probably no greater than after other therapeutic procedures.

ASPIRIN AND CALCIUM: Favourable results have been obtained for many years by the use of aspirin (e.g. gr. 10 t.d.s. for a child of 10 to 12 years). More recently calcium salts (e.g. calcium lactate) have also been used, usually in conjunction with aspirin, especially since Warner (1930) found that there was a deficiency of calcium in the serum and cerebro-spinal fluid of all his cases of active chorea, and that this was rectified at the end of the attack. Another basis for this mode of treatment was the fact that the distribution of chorea closely resembles that of rickets, in that it is most prevalent in large cities. The drug calcium aspirin has been known for many years, but it had never come into general use, being unsuitable for continued oral administration owing to its instability. However, Mutch (1934), using a new stable preparation, reported excellent results in the treatment of chorea. In 19 cases, his average daily dose varied up to gr. 45 for a child 12 years old. The average time taken to control the attacks was 17 days, and the limits 7 and 46 days respectively. He considered the condition cured when an average medical man would have had difficulty in/
in diagnosing the case as one of chorea at all. These figures have never been confirmed by other investigators. The author has seen calcium aspirin exhibited in many cases of chorea, in conjunction with as great a degree of isolation as was possible, without being impressed that the results were very much better than those obtained by the use of aspirin alone.

TOXICOTHERAPY: This term is used in preference to pyretotherapy, because pyrexia, from other than physical causes, is essentially an index of the reaction of the organism against a poison, and is thus only one, albeit an important one, of many complex changes, both cellular and humoral, produced. Pyretotherapy will be defined as, and reserved for, the treatment of disease by pyrexia produced by physical methods. Toxicotherapeutic procedures include non-specific protein therapy, the use of intramuscular injections of colloidal sulphur, and, of course, the administration of nirvanol, which has already been considered under a separate heading.
NON-SPECIFIC PROTEIN THERAPY.

This is the most important form of toxicotherapy.

HISTORICAL SURVEY: In ancient times, certain South American tribes practised the exposure of sufferers from leishmaniasis braziliensis to malarial infection. From the era of Hippocrates, who believed that malaria had a beneficial effect on epilepsy, medical observers have from time to time noted the favourable influence of certain fevers on the course of mental diseases. They have also described the actual disappearance of chronic infections after febrile attacks.

At the beginning of the 19th century, artificial suppuration was used in the treatment of dementia paralytica and other psychoses, horsehair plaits being drawn under the skin of the chest for this purpose. A little later, paretic patients were actually infected with erysipelas in an attempt to arrest the progress of the disease. Remissions occasionally resulted; death occurred often. In 1876, Rozenblum treated patients suffering from various mental disorders by the artificial production of relapsing fever.

Wagner-Jauregg (1887) after reviewing the influence of such diseases as cholera, typhoid, erysipelas, and relapsing fever on various psychoses, suggested the induction of malaria for the treatment of dementia paralytica. He did not put his suggestion into/
into practice until 1917 however, preferring in the interval to experiment with less severe pyretogenetic agents, such as milk, egg-albumen, peptone, sodium nucleinate, tuberculin, typhoid vaccine, staphylococcal emulsion, and the treponema of relapsing fever.

Mauriac (1896) used sodium nucleinate, and Fischer (1911) sterile milk, both injected intramuscularly, in the treatment of that disease. McIntosh, Fildes, and Dearden (1912) showed that the intravenous injection of saline solutions which had been made up with distilled water contaminated with bacteria and subsequently sterilised, was followed by a febrile reaction, and that syphilitic and other ulcers could be made to heal by this means. That is apparently the first instance of the use of non-specific intravenous protein therapy.

In the following year, Torres (1913) reported the successful treatment of typhoid fever by intravenous injections of typhoid vaccine, describing the sharp reactions which ensued. Subcutaneous injections of this vaccine had been previously used with no effect. In the same year, Bruck (1913) also observed that in the treatment of gonococcal infections, large intravenous doses of gonococcus vaccine were frequently followed by marked clinical improvement. Kraus and Mazza (1914) treated typhoid fever with a Bacillus coli vaccine, and obtained/
obtained results similar to those produced by typhoid vaccine, thus proving that the method was non-specific.

Since that date countless papers have been written on the treatment of numerous diseases by various non-specific protein agents. Indeed, excessive and indiscriminate enthusiasm brought the procedure into disrepute, and it is only recently that its prestige is being regained, at least in part, by reason of its gradual emergence from the chrysalis stage of empiricism, with the accumulation of knowledge regarding the fundamental nature of the reactions that follow its use.

THE REACTION AFTER THE INTRAVENOUS INJECTION OF A VACCINE.

The nature of the physiological changes produced in the organism by non-specific protein therapy has been, and is still being profoundly studied, especially in America. And rightly so, because the successful application of any therapeutic measure depends upon an understanding of the resultant physiological effects, both from a curative point of view and with the object of avoiding undesirable or even dangerous reactions.

The biological reaction evoked by an intravenous injection/
injection of killed bacteria varies enormously. It will depend upon the virulence of the antigen, and upon the functional and pathological status of the individual tissue. Tissues that are already stimulated or fatigued will respond quite differently to resting tissues. Thus diseased organs may either react more profoundly (so-called focal reaction) or less markedly than normal ones. Further, imbalanced endocrinous or nervous control may enhance or aberrate parenchymal reactivity.

Clinically, the reaction is distinctly pentaphasic:

1. Latent period of ½ to 1½ hours, sometimes longer.
2. Sooner or later general malaise sets in, followed by a chill which ushers in a rigor. There is now cold perspiration, pallid cyanosis, tachycardia, nausea, and occasionally vomiting. The radial pulse is of diminished volume and in severe reactions may become almost imperceptible.
   The brachial systolic blood pressure is lowered. This is the phase which all patients dread. It is the stage of pyretogenesis, and may last for a ½ to 2 hours or more. In chorea, the movements may be aggravated by the muscular contractions associated with the rigor.
3. The external temperature begins to rise. The patient becomes flushed and feels hot and uncomfortable. The peripheral blood volume and blood pressure increase. The latter may rise above/
above normal. There may be some sweating, frequently there is none. General malaise is lessened, but headache may be experienced. The symptoms of disease may be exaggerated. The pyrexia reaches its fastigium during this phase, which lasts 2 to 3 hours.

4. Now ensues a stage of more profuse sweating, during which the temperature gradually falls to normal with a cessation of the subjective disturbance and an abatement of the tachycardia. The average duration of this stage of defervescence is just over 3 hours. Sometimes the temperature will swing for much longer than this, showing several secondary rises, before returning to normal.

5. With the reestablishment of an apyrexial status, the patient experiences a feeling of well-being, and considerable clinical improvement may be shown, even although it may only be temporary. Not infrequently a secondary reaction may occur after an interval of 1 to 6 hours or more.

The writer's conception of the nature of the reaction is as follows.

During the 1st phase the injected organisms are absorbed by the cells of an activated reticulo-endothelial system (Saxl, 1926), largely in the liver and spleen, with a resultant stimulation of the regional parenchyma. The regional defences sooner or later prove to be inadequate/
inadequate.

A generalised parenchymal stimulation is then initiated, with a summoning of the general defensive forces, and a mobilisation of reserves. A primary status of "secondary shock" is enforced to this end, and to segregate the endotoxins, probably by the nervous release of histamine-like substances.

Dale and Laidlaw (1919) have shown that histamine will produce symptoms identical with those of shock, and that a histamine-like substance can be obtained from most of the bodily tissues.

Freund and Gottlieb (1922) have actually isolated a vasodilatory substance from the blood immediately after the onset of the protein reaction.

A greater or lesser amount of the circulating blood is accordingly impounded in the splanchnic vascular field, with a proportionate diminution of the peripheral volume. While the assembling of antitoxin reserves from the tissues is facilitated by a stasis of blood in dilated and augmented capillaries of increased permeability, and by an increase of the lymph flow. This capillary stasis is aided by contraction of the arterioles, and the increased lymph flow by the muscular contractions associated with the rigor. The diminution in volume of circulating blood is aided by the loss of a certain amount of plasma through the capillary walls.
During the whole of this period the action of the heart remains strong and regular. The association of increased metabolic activity with the diminution of heat loss effected by the reduced peripheral circulation causes an internal elevation of temperature.

The advent of the 3rd phase is an indication that the defensive mechanisms have been prepared for action, and that the battle is being joined in earnest. The warring forces are swept into action as the peripheral circulation is reactivated. The surface temperature rises. Although the skin becomes flushed with the relaxation of the arterioles, the sweat glands are often inhibited in some way, and the heat loss is still insufficient to compensate for the increased production.

The symptoms of disease may be exaggerated owing to the stimulation of inflammatory foci of infectious and non-infectious origin. This constitutes the so-called focal reaction ("herdreaktion").

In the 4th phase the endotoxins become neutralised. The loss of heat is increased by sweating, and the temperature gradually falls.

The contest is over.

According to Petersen and Müller (1927) the reaction is essentially diphasic, with a primary phase associated with a parasympathetic splanchnic and a sympathetic/
sympathetic peripheral status, and a secondary phase in which the splanchnus-peripheral balance is reversed, the splanchnic region becoming sympathetically and the periphery parasymptatically orientated.

Numerous changes have been noted in the tissues and in the blood with but little comprehension of their relative therapeutic significance. Unfortunately little animal experimentation seems to have been attempted to this end, even although it is now over 40 years ago since Pfeiffer and Issaef (1894) found that non-specific injections temporarily raised the resistance of guinea-pigs to cholera.

Some of the more important of the peripheral blood changes reported are:

1. A leucopenia followed by a leucocytosis.
   This was first noted by Lange (1903).
   Holler (1915) showed that the leucocytosis is caused by cells of the granular series, and that there is a shift to the left in the Arneth count. Whether these granulocytes have a greater phagocytic power has not been determined.

2. A diminution then an increase of proteolytic and lipolytic ferments (Jobling and Petersen, 1915).

3. A reduction then an increase in non-protein nitrogen (Jobling and Petersen, 1915).

5. A shortening of the sedimentation rate, and a diminution of the coagulation time in the secondary phase (Schmidt and Kaznelson, 1916). This is probably associated with an increase of fibrinogen, demonstrated by Kapoczweski (1925) who also showed that there was a primary reduction.

6. A transient alkalosis (Lukacs, 1926) then an acidosis, with a secondary alkalosis (Eggstein, 1921).

7. Hoff and Silberstein (1925) have shown that the opsonic index for staphylococci, streptococci, and B. coli is increased in the serum and C.S.F. during malarial-therapy and after the completion of treatment.

8. A diminution then an increase of complement. (Malkin, 1926).

9. A reduction then an increase in the Ca-K ratio. (Petersen and Müller, 1927).

Among the organic changes reported, Müller and Petersen (1927) have shown that during the primary phase the stomach secretes an acid gastric juice and dilates.

Henceforward, phase 1 of the febrile reaction will be considered as the period from the onset of pyrexia to the fastigium, and phase 2 as the period of defervescence.
APPLICATION IN CHOREA.

It has long been a well-recognised clinical fact that an intercurrent infection will often cause a definite improvement in the symptoms of chorea. Horton (1922) seems to have been the first to apply this knowledge therapeutically. He successfully treated 2 cases of chorea by intravenous injections of a chemically pure protein, prepared from ox-blood fibrin by peptic and hydrochloric acid digestion.

Von Kern (1923) reported 3 cases of severe chorea which recovered soon after receiving intramuscular injections of milk. Hymanson (1926) injected boiled milk intramuscularly in 7 cases with good results. Somogyi (1927) also used this method with favourable results. Mas de Ayala (1930) described the rapid improvement obtained in a severe case by inoculation with Treponema hispanicum. In the following year Sutton (1931) published a series of cases in which she obtained remarkably successful results by the use of a T.A.B. vaccine given intravenously. This series has since been enlarged and controlled by Sutton and Dodge (1933 and 1936). Their vaccine contains 1000 million B. typhosi and 750 million each of B. paratyphosi A. and B. per c.c. They begin with a dose of 125 million/
million or 250 million organisms and treatment is continued daily, with occasional days of rest, until all signs of chorea have gone. The dosage is determined by the reaction of the patient to the previous injection. In general the dose is doubled each time unless the previous pyrexia was high, in which case it is only increased by half as much again. A temperature of about 104°F is desirable, and if necessary, a second smaller dose is given the same day to attain this result. The authors say that it is generally easy to decide when an attack is over. In doubtful cases, where there may be difficulty in deciding whether incoordination is due to weakness or to chorea, the child receives massage and occupational therapy. If the weakness decreases with the increase of activity, the attack is considered over. 150 cases have been treated, and they are divided into 3 groups - mild, moderate, and severe - according to the severity of the movements. 150 controls, treated by ordinary routine methods, are also listed. The average duration of a mild attack was reduced from 27.4 days (48 cases) to 5.72 days (68 cases); of a moderate attack, from 44.0 days (68 cases) to 8.56 days (57 cases); of a severe attack, from 62.4 days (33 cases) to 15.8 days (25 cases). Thus in the whole series of 300 cases, the average duration of an attack of chorea was reduced from 42.6 days to 8.5 days, an improvement/
improvement of 401%. It is not stated whether any refractory cases were encountered or included in the results. Other workers using T.A.B. vaccine have not been able to confirm these figures.

Thus Capper and Bauer (1933) treated 23 cases, dividing them into 3 classes - acute (onset up to 2 weeks before admission), subacute (up to 6 months), and chronic (over 6 months). They aimed at producing a temperature of 102°-104° F. and commenced with a dose of 150 or 200 million organisms. The injections were continued daily for 6 or 7 days on the average (the dose being usually increased by 100 million each time), then a rest period of several days was instituted. When the child did not recover after the 1st series of injections, then a 2nd, 3rd, or even 4th series were given. Decided improvement was usually noticeable after the 2nd or 3rd injection, and an average of 12.48 were given. 19 of the 23 cases were discharged from hospital free of symptoms. Of the remaining 4 cases, one showed no improvement, another blinked persistently, a third was persistently talkative, and the fourth had to be prematurely discharged because of an intercurrent infection. The duration of the attack was given definitely only in 15 cases, the average being 17.74 days. This figure would have been appreciably raised by the inclusion of the other cases.

Monfort (1934) published a series of 23 cases in which/
which the average duration of the attack was just over 16\(\frac{1}{2}\) days.

Ash and Einhorn (1935) gave 17 patients an average of 7.35 daily injections and classified the resultant improvement as rapid, (4 cases); gradual, (5 cases); and very gradual, (2 cases). No improvement was observed in 2 cases, no result was given in another 3 cases, and a relapse occurred in hospital in one case.

Litchfield, Gillman, Harris, and Cohen (1936) reported the treatment of 8 cases by daily injections. They stated the definite duration of the attack in only 2 cases (10 days and 4 weeks), and in another 4 noted considerable improvement after an average of 15.5 days. There was one poor result, and injections were stopped in another case owing to the severity of the 1st reaction.

Other methods of non-specific protein therapy, which have been used in the treatment of chorea, include malarial inoculation and intravenous injections of Nicolle's Ducrey bacillus vaccine ("dmelcos").
PYRETO THERAPY.

This is no recent therapeutic measure, for hyperthermia, physically produced by bed-warmers, and by the prevention of sufficient loss of bodily heat due to warm humid atmospheres and to the insulation conferred by bed-clothes and garments, has always been used in the treatment of disease. In the same way, hot baths have employed since time immemorial. In 1927 Neymann began experiments with diathermy in the treatment of dementia paralytica, and a technique was evolved, in collaboration with Osborne and Holmquest, giving startlingly successful results (Neymann and Osborne, 1931).

Following upon this report, an avalanche of papers have been published, mostly in America, claiming good results in diverse diseases by divers physical pyretogenetic methods. These have rather tended to discredit the procedure, owing to its experimental and uncritical application in many instances.

(7) Hydropyretogenic methods: (a) hot baths; (b) hot sprays.

The first method is that most generally employed now, especially by means of a proprietary cabinet, or "hot box", called the Kettering hypertherm. Schnabel and Fetter (1935) used this method in 12 cases of chorea, giving an average of 4 treatments bi-weekly. 9 patients were cured, 2 markedly improved, 1 moderately improved, and 1 died after a violent reaction. The average duration of the attack in the 9 cured cases was not stated, although presumably it was in the region of 14 days.

Neymann, Blatt, and Osborne (1936) have applied electropyretotherapy to the treatment of chorea with good results, in a series of 25 cases, of which 9 were very severe, 6 moderately severe, and 10 comparatively mild. They use the method of electromagnetic induction by high frequency currents to raise the temperature to 103.5° F., then switch off the current. The temperature usually rises another degree or so higher and it is maintained at this level for 7 - 8 hours by insulating the patient in a "treatment bag" or in an air-conditioned cabinet.

The choreiform movements ceased in all cases after a series of bi-weekly treatments (average 4; extremes 10 and 2), and the average period of hospitalisation was slightly less than 16 days (extremes 39 and 5). The relapse rate was 24% within a period of 1 to 20/
20 months.
Lowenburg and Nemser (1936) report the treatment of 3 cases by the use of hot baths. They slowly heat the water up to 103° - 104° F. within 20 to 30 minutes and keep the patient immersed at this temperature for at least 2 hours, preferably 3. This procedure is carried out daily at first, then at gradually longer intervals. Twelve baths usually suffice they claim.

THE METHOD USED IN THE PRESENT SERIES OF 25 CASES.

A Bacillus coli vaccine, sold under the proprietary name of "pyrifer", was the agent used to apply non-specific protein therapy to the present series of 25 cases of Sydenham's chorea. It was chosen in preference to T.A.B. vaccine because, in the experience of the author, it produces at least as good a reaction, and very rarely a violent one such as not infrequently occurs after the injection of T.A.B. vaccine, even to the point of arousing considerable anxiety. Further, it is often difficult to maintain a good reaction after several doses of the latter vaccine.

Pyrifer is made up in 1 c.c. ampoules of 7 different strengths.
1. 50 million B. coli per c.c.
2. 100 " " " " ""
3. 200 million B. coli per c.c.
4. 500 " " " .
5. 1000 " " " .
6. 2000 " " " .
7. 5000 " " " .

**MODE OF ADMINISTRATION.**

The patient is isolated as much as the available accommodation permits. One pillow is allowed. A thorough physical examination is made. Contraindications to treatment are excluded. These were considered to be:

1. Uncompensated cardiac disease. Compensated lesions were not considered contraindications.
2. General debility, if pronounced.
3. History of protein hypersensitivity.
4. Tuberculosis.

The sedimentation rate of the blood in one hour is determined, and a white blood count may be taken. On the day treatment is commenced, breakfast is not withheld. An injection of 50 million organisms is given intravenously 3 to 4 hours later.

When the rigor commences, the patient is placed in a blanket bed and supplied with several hot-water bottles.

A most careful observation by the nursing staff is now/
now maintained.
The pulse-rate and temperature are taken every 
\(\frac{1}{2}\) hour, or oftener, if the condition of the patient. 
seems to warrant it.

Copious glucose drinks are allowed, with the 
addition of some sodium bicarbonate if vomiting is 
threatened.

Tepid sponging is carried out during the hot phase 
if the temperature rises above 105° F.

With the advent of more profuse sweating, glucose 
saline drinks are given.

Adrenalin m.10 are injected hypodermically should 
the pulse become weak, or the rate rise above 160 
per minute.

The subsequent dosage of pyrifer is calculated as 
the amount thought necessary to evoke a pyrexial 
fastigium of 102° to 104° F. In general, succeeding 
strengths of the vaccine are given, but if the 
previous reaction has been severe, then only half 
as much again is allowed. The injections are 
stopped as soon as the involuntary movements are 
no longer obvious.

Four methods of estimating the B.S.R. were used: 
(1) Wintrobe's, (2) Cutler's, (3) Westergren's, 
(4) a micro-method, modified from Westergren's macro-
method. A Balaowsky's tube is used, with a 3.8% soln. 
of sod.citrate as the anticoagulant. 0.04 c.c. of the 
anticoagulant is drawn into the tube and the column is 
made up to 0.2 c.c. by blood drawn from a puncture 
wound.
THE LIST OF CASES TREATED.

The cases are divided into 3 groups - mild, moderate, and severe - according to the clinical severity of the disease.

1. Mild chorea, in which the movements are seen chiefly on voluntary effort. Speech is not definitely affected, and the patient can feed and dress himself with greater or less difficulty.

2. Moderate chorea, in which the movements are very obvious and the patient is hardly ever still. He cannot feed or dress himself, although coarse voluntary movements can still be performed. Speech is definitely affected.

3. Severe chorea, in which the movements are so violent that all purposeful voluntary action is prevented. Speech is grossly affected. Bed boards and other protective measures are required.

Each case will also be considered acute, subacute, or chronic according to the stage the disease had reached before treatment was commenced.

The acute stage is taken as the period up to 2 weeks, the subacute stage between 2 weeks and 6 months, and the chronic stage over 6 months.

The disease was considered cured clinically when all involuntary movements had ceased, voluntary movements were coordinated, and the posture of the outstretched upper limbs was normal.
THE SERIES TREATED BY PYRIFER INJECTIONS.

GROUP 1 - MILD CASES.

A. ACUTE.

CASE 1.

Female, aged 13.

Family history of tuberculosis.

Past History: Occasional sore throat.

Onset of Chorea: 5 days before admission.

Examination: Mild degree of chorea; generalised.

- General condition good.
- Pulse-rate 90 per minute.
- Temperature 97.2° F.
- Tonsils enlarged. Several carious teeth.
- Heart: N.A.D.
- B.S.R. (Cutler) 10.0 mm.
- White blood count 5,600; granulocytes 4,816 and lymphocytes 784.

Treatment: Patient isolated.

Injections of pyrifer started on the day after admission; 7 given.

Progress: Symptoms relieved 23 days after the 1st reaction; 9 days after the last one.

The B.S.R. 2 months later had fallen to 3.0 mm.

The patient was discharged 22-23 weeks after admission. No reply was received to an enquiry re her health 8 months later.
Febrile Reactions: Average duration $8\frac{1}{2}$ hours.
1st phase 4 hours; 2nd phase $4\frac{1}{2}$ hours.
Highest temperature attained - 103.2° F.
Average temperature peak - 101.9°F.
Fastest pulse-rate 136 per minute.

B. SUBACUTE.

CASE 2.

Female, aged 8.
Family history of rheumatism.
Past History: Chorea at age of 6.
Scarlet fever the following year.
Onset of Present Chorea: 11 weeks before admission,
immediately preceded by an attack of 'growing pains'.
Examination: Mild degree of chorea; generalised.
General condition fair.
Pulse-rate 100 per minute.
Temperature 98.0°F.
Apex-beat forcible and in mid-clavicular line. Mitral systolic bruit present,
propagated into the left axilla.
Pulmonary 2nd sound accentuated.
B.S.R. (Micro-method) 22.0 mm.

Treatment: Patient isolated.
Pyrifer injections commenced 3 days after admission; 4 given.
Progress: Chorea clinically cured 16 days after the/
the first reaction; 10 days after the last one. After many weeks of rest in bed, the apex-beat came within the mid-clavicular line, but the character of the bruit remained the same.

The B.S.R. 4 months later had fallen to 2.5 mm. The patient was discharged during the 26th week after admission. She had an attack of acute rheumatism at home 1 month later, and there was a recurrence of chorea about 10 months after this.

Febrile Reactions: Average duration 5 hours.

1st phase 2 hours; 2nd phase 3 hours.

Highest temperature attained - 103.0°F.

Average temperature peak - 102.3°F.

Fastest pulse-rate 156 per minute.

CASE 3.

Female, aged 11.

Family history of rheumatism.

Past History: nil relevant.

Onset of Chorea: 3 weeks before admission.

Examination: Mild degree of chorea; generalised.

General condition good.

Pulse-rate 112 per minute.

Temperature 98.2°F.

Heart; N.A.D.
B.S.R. (Micro-method) 15.0 mm.

Treatment: Patient isolated.

Pyrifer injections commenced 7 days after admission; 5 given.

Progress: Symptoms disappeared 14 days after the first reaction; 4 days after the last one.
The B.S.R. fell to 2.5 mm. 3 months after admission. The patient was discharged 10 weeks later. No reply was received to an enquiry re her health some 9 months afterwards.

Febrile Reactions: Average duration 4 hours.

1st phase $1\frac{1}{2}$ hours; 2nd phase $2\frac{1}{2}$ hours.

Highest temperature attained - 102.8°F.

Average temperature peak - 100.7°F.

Fastest pulse-rate 134 per minute.

CASE 4.

Male, aged 9.

Family history of rheumatism.

Past History: Acute rheumatism 1 year before admission; in bed for 7 months.

Onset of Chorea: 5 days before admission.

Examination: Mild degree of chorea, affecting the face and upper limbs.

General condition good.

Pulse-rate 96 per minute.
Temperature 97.8°F.
Heart: N.A.D.
B.S.R. (Cutler) 2.0 mm.

Treatment: Symptoms so mild that rest in bed was the only form of treatment given for the first week; no improvement however. Patient isolated during the next 11 days but no improvement noted.
Pyrifer injections commenced on the 19th day after admission; 7 given.

Progress: After the 7th reaction, only an occasional grimace or slight purpose-like movement noted, and then only when the patient knew he was under observation. Symptoms disappeared 9 days later. The patient was discharged 20 weeks after admission. No recurrence of symptoms within just over 7 months.

Febrile Reactions: Average duration 4½ hours.
1st phase 2½ hours; 2nd phase 2 hours.
Highest temperature attained - 102.4°F.
Average temperature peak - 101.1°F.
Fastest pulse-rate 144 per minute.
C. CHRONIC.

CASE 5.

Male, aged 12.
Family History : nil relevant.
Past History : nil relevant.
Onset of Chorea : 4 weeks before admission.
Examination : Chorea moderately severe, more pronounced on the left side.
General condition fairly good.
Cerebration sluggish.
Pulse-rate 76 per minute.
Temperature 97.2°F.
Tonsils enlarged, also several cervical glands.
Heart : N.A.D.
B.S.R. (Cutler) 5.0 mm.
Treatment : 3 febrile reactions were induced by means of a T.A.B. vaccine, first 20 million organisms, then 40 million, and again 40 million. Movements were considerably diminished. 5 months later, a mild degree of chorea still being present, pyrifer injections were starter; 2 given.
Progress : Symptoms disappeared after the 2nd reaction. Hypotonia of the muscles of the upper limbs and a slight degree of grimacing reappeared however within
a/
a day or two, but permanently went after a further 13 days. The patient was discharged 32 weeks after admission. No recurrence of symptoms within $16\frac{1}{2}$ months.

CASE 6.

Female, aged 9.

Family History: nil relevant.

Past History: Scarlet fever when aged 7.

Onset of Chorea: 6 weeks before admission.

Examination: Mild degree of chorea; generalised.

General condition fair.

Cerebration normal.

Pulse-rate 88 per minute.

Temperature 97.0°F.

Heart: N.A.D.

B.S.R. (Cutler) 9.0 mm.

Treatment: Nirvanol gr. 5 daily exhibited until a morbilliform rash appeared on the 9th day; no improvement noted. Calcium aspirin gr.10 t.d.s. now tried; slow improvement noted. After several months, T.A.B. vaccine was used; two intravenous injections of 40,000 organisms given; considerable improvement noted. Patient first seen by me 12 months/
months after admission; there was still a mild degree of chorea present. Isolation ordered and pyrifer injections started; 4 given.

Progress: After the 4th reaction symptoms so mild that no further injections given. They did not disappear entirely however for another 64 days. The patient was discharged 18 months after admission, only to be readmitted 9 months later suffering from another attack. This time there were definite signs of active rheumatic endocarditis.

Febrile Reactions: Average duration 4 hours.

1st phase 1½ hours; 2nd phase 2½ hours.

Highest temperature attained - 102.4°F.

Average temperature peak - 102.0°F.

Fastest pulse-rate 152 per minute.
GROUP 2 - MODERATE CASES.

A. ACUTE.

CASE 7.

Female, aged 12.
Family History: nil relevant.
Past History: 'Meningitis' as a child.
Onset of Chorea: 1 week before admission.
Examination: Chorea of moderate severity; more pronounced on the right side.
General condition good.
Tonsils enlarged. Several carious teeth present.
Pulse-rate 80 per minute.
Temperature 98.0°F.
Faint systolic apical murmur; no accentuation of the 2nd sound. Apex-beat internal to the mid-clavicular line.
B.S.R. (Micro-method) 10.0 mm.

Treatment: Patient isolated. Little change in the condition after 6 days.
Pyrifer injections commenced on the 7th day; 4 given.

Progress: Symptoms very mild after the 4th reaction and they disappeared 4 days later.
The B.S.R. shortened to 30.0mm. during the/
the course of injections, then lengthened to 2.0 mm. 7 weeks later. The patient was discharged during the 26th week after admission. A recurrence of symptoms was noted however some 7 months later.

Febrile Reactions: Average duration 3 hours.
1st phase 1½ hours; 2nd phase 1½ hours.
Maximum temperature - 103.2°F.
Average temperature peak - 101.0°F.
Fastest pulse-rate 148 per minute.

B. SUBACUTE.

CASE 8.

Male, aged 11.
Family History: nil relevant.
Past History: occasional tonsillitis.
Onset of Chorea: 4 weeks ago.
Examination: Chorea moderately severe; more pronounced on the left side.
General condition good.
Cerebration slow.
Pulse-rate 58 per minute.
Temperature 97.8°F.
Tonsils enlarged.
Cervical lymph glands enlarged.
Heart: N.A.D.
Treatment: Patient isolated. Calcium aspirin gr. 10 t.d.s. given for 12 days; improvement moderate. On the 13th day, pyrifer injections started; 4 given.

Progress: Symptoms practically gone after the 4th reaction. None present 19 days later, i.e. 27 days after the first injection. The patient was discharged on the 78th day after admission.

No reply was received to an enquiry re the health of the child 14 months later.

CASE 9.

Male, aged 9.

Family History: nil relevant.

Past History: Acute rheumatism at the age of 4.

Chorea when aged 7, the patient being hospitalised for over 7 months.

Onset of Present Chorea: 12 weeks before admission.

Examination: Moderately severe degree of chorea, affecting the left side only.

General condition fairly good.

Pulse-rate 78 per minute.

Temperature 98.0°F.

Heart not enlarged. Systolic murmur audible over the mitral and pulmonary areas. Slight accentuation of the pulmonary 2nd sound.
Treatment: Ca.aspirin gr.10 t.d.s. exhibited for 12 days; little improvement noted. The patient was isolated a few days after admission; definite lessening of the frequency of the movements resulted. On the 13th day, treatment with pyrifer was commenced; 12 injections given.

Progress: Symptoms relatively mild after the 6th reaction, and almost clear by the 12th one. They disappeared 15 days later. The systolic bruit persisted, but the cardiac response to effort was good. The patient was discharged on the 99th day after admission. No reply was received to an enquiry re the health of the child 13 months later.

Febrile Reactions: Average duration 4\(\frac{1}{2}\) hours. 1st phase 2 hours; 2nd phase 2\(\frac{1}{2}\) hours. Highest temperature attained - 104.4°F. Average temperature peak - 103.1°F. Fastest pulse-rate 148 per minute.

CASE 10.

Female, aged 13.

Family History: nil relevant.

Past History: Tonsillectomy during early childhood.
Onset of Chorea: 4 weeks before admission.

Examination: Chorea moderately severe; generalised.
General condition good.
Pulse-rate 80 per minute.
Temperature 97.8°F.
Heart: N.A.D.
B.S.R. (Cutler) 10.5 mm.

Treatment: Calcium aspirin exhibited for 6 days
with no effect. Pyrifer injections
commenced on the 7th day; 6 given.

Progress: Symptoms very mild after the 6th
reaction; they disappeared 11 days
later.
B.S.R. (Micro-method) lengthened to
5.0 mm. within 3 months. The patient
was discharged in the 20th week after
admission.

Febrile Reactions: Average duration 3 hours.
1st phase 2 hours; 2nd phase 1 hour.
Highest temperature attained - 105.0°F.
Average temperature peak - 102.5°F.
Fastest pulse-rate 140 per minute.

CASE 11.

Female, aged 11.

Family History: nil relevant.

Past History: Two previous attacks of chorea, one
at the age of 7; the other when aged 9, preceded by joint pains and complicated by scarlet fever.

Onset of Present Chorea: 11 weeks before admission.

Examination: Chorea moderately severe; generalised.

General condition fairly good.

Pulse-rate 82 per minute.

Temperature 97.2°F.

Tonsils enlarged.

Cervical lymph glands enlarged.

Apex-beat inside the mid-clavicular line. Systolic bruit audible, loudest in the pulmonary area. No accentuation of the pulmonary 2nd sound.

Treatment: Patient not isolated.

Fyrifer injections commenced 4 days after admission; 5 given.

Progress: By the 5th reaction, symptoms had become mild, but they did not entirely disappear until after the lapse of a further 49 days.

The B.S.R. (Micro-method), taken during the course of injections, was 32.0 mm. When taken 2 months later it had lengthened to 3.0 mm. The cardiac bruit disappeared about this time. The patient was discharged during the 35th week after admission. No recurrence of symptoms within 11 months.
Febrile Reactions: Average duration 3 hours.

Both phases 1½ hours.
Highest temperature attained - 102.8°F.
Average temperature peak - 102.0°F.
Fastest pulse-rate 138 per minute.

CASE 12.

Male, aged 9.

Family History: nil relevant.
Past History: nil relevant.

Onset of Chorea: 2 weeks before admission, accompanied by a sore throat. Transient joint pains were experienced a week later.

Examination: Chorea of moderate severity; generalised.

General condition fairly good.
Pulse-rate 108 per minute.
Temperature 97.4°F.
Heart: N.A.D.
B.S.R. (Cutler) 2.5 mm.

Treatment: Patient isolated.
Pyrifer injections commenced 2 days after admission; 6 given.

Progress: Mild symptoms persisted for 42 days after the 6th reaction. Patient sent to school during the last week.
The patient was discharged during the 14th week after admission. No recurrence/
currence of symptoms within 9 months.

Febrile Reactions: Average duration 5 hours.
1st phase 2 hours; 2nd phase 3 hours.
Highest temperature attained - 103.0°F.
Average temperature peak - 101.5°F.
Fastest pulse-rate 144 per minute.

CASE 13.

Male, aged 11
Family history of tuberculosis.
Past History: nil relevant.
Onset of Chorea: 3 weeks before admission.
Examination: Chorea moderately severe; generalised.
General condition good.
Pulse-rate 92 per minute.
Temperature 99.0°F.
Cervical glands enlarged; no tonsillar enlargement.
Systolic cardiac bruit present, loudest in the pulmonary area; accentuation of the 2nd sound. Apex-beat inside the mid-clavicular line.
B.S.R. (Wintrobe) 10.0 mm.

Treatment: Patient isolated.
Pyrifer injections commenced on the day after admission; 5 given.

Progress: After the 5th reaction, symptoms very mild,
mild, but they did not disappear for a further 18 days. The cardiac bruit disappeared within a month, and the B.S.R. lengthened to 2.0 mm.
The patient was discharged during the 16th week after admission. No recurrence of symptoms within 8 months.

Febrile Reactions: Average duration 5 hours.
1st phase 2 hours; 2nd phase 3 hours.
Highest temperature attained - 105.0°F.
Average temperature peak - 103.2°F.
Fastest pulse-rate 140 per minute.

CASE 14.

Female, aged 8.
Family history both of rheumatism and of tuberculosis.
Past History: Acute rheumatism 1 year ago.
         Tonsillitis 6 months later.
Onset of Chorea: 3 weeks before admission.
Examination: Chorea of moderate severity; generalised.
         General condition fair.
         Pulse-rate 92 per minute.
         Temperature 97.0°F.
         No tonsillar enlargement.
         Systolic and mid-diastolic mitral murmurs present, the former being propagated into the left axilla.
         Pulmonary 2nd sound accentuated.
Apex-beat internal to the mid-clavicular line.

B.S.R. (Micro-method) 41·0 mm.

Treatment: Patient isolated.

Pyrifer injections started on the day after admission, there being no evidence of cardiac insufficiency at rest; 5 given.

Progress: Symptoms cleared up 2 days after the 5th reaction; 10 days after the first one. Cardiac condition unaltered. The B.S.R. lengthened to 100 mm. in just over 3 months. The patient is still in hospital under treatment for the rheumatic endocarditis. No recurrence of choreic symptoms within 8 months.

Febrile Reactions: Average duration 5½ hours.

1st phase 2 hours; 2nd phase 3½ hours. Highest temperature attained - 103·2°F. Average temperature peak - 102·4°F. Fastest pulse-rate 146 per minute.
C. CHRONIC.

CASE 15.

Female, aged 9.
Family History: nil relevant.
Past History: nil relevant.
Onset of Chorea: 12 months before admission. After the first two or three months, the symptoms became relatively mild, but an exacerbation occurred a few weeks ago.

Examination: Chorea moderately severe; most pronounced in the right upper limb. General condition fairly good. Pulse-rate 100 per minute. Temperature 97.6°F. Heart: N.A.D. B.S.R. (Micro-method) 9.0 mm. White blood count 7,800; granulocytes 3,042 and lymphocytes 4,290.

Treatment: Patient isolated. No other treatment given for 20 days; improvement very slight. Pyrifer injections accordingly commenced on the 21st day; 4 given.

Progress: After the 4th reaction symptoms were very mild, but they persisted for another 57 days. The patient was discharged/
discharged during the 14th week after admission. No recurrence of symptoms within 11 months.

Febrile Reactions: Average duration 8 hours. Both phases 4 hours.
Highest temperature attained - 103.4°F.
Average temperature peak - 101.9°F.
Fastest pulse-rate 176 per minute (on this occasion adrenaline m.10 was given, the pulse volume being poor).

CASE 16.

Male, aged 8.
Family History: nil relevant.
Past History: nil relevant.
Onset of Chorea: 12 months ago. The condition became very mild after a few months, but latterly has become worse again.

Examination: Moderately severe degree of chorea; more pronounced on the left side.
General condition fairly good.
Pulse-rate 92 per minute.
Temperature 97.0°F.
Heart: N.A.D.
B.S.R. (Wintrobe) 1.0 mm.
White blood count 3,800; granulocytes 2,052 and lymphocytes 1,406.
Treatment: Patient isolated.

Pyrifer injections commenced 4 days after admission; 6 given.

Progress: Symptoms very mild after the 6th reaction. They disappeared 11 days later. The patient was discharged on the 41st day after admission.

No recurrence of symptoms within 12 1/2 months.

Febrile Reactions: Average duration 3 1/2 hours.

1st phase 1 1/2 hours; 2nd phase 2 hours.

Highest temperature attained - 103.8°F.
Average temperature peak - 101.7°F.

Fastest pulse-rate 160 per minute.
GROUP 3 - SEVERE CASES.

A. ACUTE.

CASE 17.

Male, aged.

Family History: nil relevant.
Past History: nil relevant.

Onset of Chorea: 1 week ago, accompanied by a sore throat.

Examination: Severe degree of chorea; generalised.
  General condition good.
  Pulse-rate 62 per minute.
  Temperature 97.0°F.
  Tonsils enlarged.
  Heart: N.A.D.

Treatment: Calcium aspirin gr.15 t.d.s. given for a week with little effect.
  Patient isolated a few days after admission with definite lessening of the severity of the choreiform movements. On the 8th day, treatment with pyrifer commenced; 8 injections given.

Progress: The gross movements quickly abated and all signs of chorea had disappeared 23 days after the first injection and 8 days after the last one.
The patient was discharged on the 55th day after admission. No recurrence of symptoms within 15\(\frac{1}{2}\) months.

Febrile Reaction: Average duration \(7\frac{1}{2}\) hours.
1st phase \(2\frac{1}{2}\) hours; 2nd phase 5 hours.
Highest temperature attained - 104.2°F.
Average temperature peak - 103.3°F.
Fastest pulse-rate 144 per minute.

CASE 18.

Female, aged 21.
Family history of rheumatism and chorea.
Past History: Tonsillitis, diphtheria, and scarlet fever at the age of 9. Attack of chorea when aged 19; severe in degree; recovery occurred after about 8 months. Second attack 2 months later; recovery took 7 months this time.
Onset of Present Chorea: 1 week before admission.
Examination: Severe degree of chorea; generalised.
General condition fairly good.
Pulse-rate 96 per minute.
Temperature 98.0°F.
Deep reflexes very active.
Heart: N.A.D.
B.S.R. (Micro-method) 2.0 mm.
Treatment: Patient isolated.
Pyrifer injections commenced 2 days after/
after admission; 5 given.

**Progress:** Symptoms entirely disappeared after the 5th reaction. The B.S.R. increased after 4 days to 16.0 mm., then returned to 5.0 mm. in another month. The patient was discharged 17 weeks after admission. No recurrence of symptoms within 10\(\frac{1}{2}\) months.

**Febrile Reactions:** Average duration 7 hours.

1st phase 3 hours; 2nd phase 4 hours.

Highest temperature attained 105.0°F.

Average temperature peak - 102.6°F.

Fastest pulse-rate 138 per minute.

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**B. SUBACUTE.**

**CASE 19.**

**Male,** aged 6.

**Family History:** nil relevant.

**Past History:** Treated in this hospital for rickets 3 years ago.

Onset of Chorea: 3 weeks ago following the extraction of some decayed teeth.

**Examination:** Chorea severe; generalised.

General condition fair.

Cerebration only fair.

Pulse-rate 72 per minute.

Temperature 97.2°F.
Tonsils enlarged.
Heart; N.A.D.
B.S.R. (Wintrobe) 10.0 mm.

**Treatment**: Patient isolated. Pyrifer injections commenced 2 days after admission; 11 given.

**Progress**: Symptoms slow to subside; disappeared 39 days after the first reaction and 20 days after the last one.
The patient was discharged on the 60th day after admission. No recurrence of symptoms within 13½ months.

**Febrile Reactions**: Average duration 6 hours.
Both phases 3 hours.
Highest temperature attained - 104.0°F.
Average temperature peak - 101.5°F.
Fastest pulse-rate 146 per minute.

**CASE 20.**

Female, aged 7.
Family history of rheumatism.
Past History: Attack of chorea 2 years ago.
Onset of Present Chorea: 3 weeks before admission.
Examination: Very severe degree of chorea;
generalised.
General condition fair.
Pulse-rate 80 per minute.
Temperature 97.0°F.
Dental caries pronounced.
Apex-beat in the mid-clavicular line.
Systolic apical murmur present:
Pulmonary 2nd sound accentuated.
B.S.R. (Cutler) 15.5 mm.

**Treatment**: Pyrifer injections commenced on the
day after admission; 7 given.
Patient not isolated.

**Progress**: Symptoms relatively mild after the 5th
reaction, and cleared up 24 days after
the 7th one. The cardiac condition
improved during the next few months
and the B.S.R. lengthened to 7.0 (Micro-
method). 4 months later however, there
was a recurrence of the chorea. Symptoms
were of moderate severity this time.
They quickly improved after isolation,
and disappeared in 2 months. During
the preceding month, the cardiac bruit
had no longer been audible.

**Febrile Reaction**: Average duration 7 hours.

1st phase 3 hours; 2nd phase 4 hours.
Highest temperature attained - 104.6°F.
Average temperature peak - 103.0°F.
Fastest pulse-rate 152 per minute.
CASE 21.

Male, aged 12.

Family History: nil relevant.

Past History: Tonsillitis at age of 4.

Onset of Chorea: 10 weeks before admission. Symptoms getting worse latterly.

Examination: Severe degree of chorea; generalised.

Obese type.

General condition good.

Cerebration sluggish.

Pulse-rate 110 per minute.

Temperature 97.4°F.

Tonsils enlarged. No enlarged cervical glands.

Systolic bruit present, loudest in the pulmonary area; no accentuation of the pulmonary 2nd sound. Apex-beat within the mid-clavicular line.

Treatment: Patient isolated.

Pyrifer injections commenced on the day after admission; 8 given.

Two reactions were rather severe.

Adrenaline m.10 had to be given hypodermically during the rigor on these occasions, the peripheral circulation having become very embarrassed, with pronounced cyanosis, pulse of poor volume, and tachycardia of over 106 per minute.
Progress: Symptoms slow to improve. They were relatively mild after 8 reactions, but did not disappear until after a further 39 days. A faint cardiac bruit persisted.

The B.S.R. (Wintrobe) was 45·0 mm. during the course of injections; other readings have been mislaid.

The patient was discharged 3 months after admission. No recurrence of symptoms within 8 - 9 months.

Febrile Reactions: Average duration 7½ hours.
1st phase 2 hours; 2nd phase 5½ hours.
Highest temperature attained - 104·8°F.
Average temperature peak - 103·7°F.
Fastest pulse-rate 150 per minute.

CASE 22.

Male, aged 7.

Family History: nil relevant.

Past History: Tonsillectomy 2 years ago. Acute rheumatism 1 year ago followed, 2 months later, by an attack of chorea. This lasted 3 months.

Onset of Present Chorea: 5 weeks before admission; symptoms increasing latterly.

Examination: Severe degree of chorea; generalised.
General condition fairly good.

Pulse-rate 132 per minute.

Temperature 100.0°F.

No enlarged cervical glands.

Apex-beat just internal to the mid-clavicular line and localised. Mitral systolic murmur present, propagated to the other cardiac areas and into the left axilla. Pulmonary 2nd sound accentuated.

Treatment: Patient isolated.

Pyrifer injections commenced on day of admission; 4 given.

Progress: Symptoms disappeared 3 days after the last reaction; 10 days after the first one.

The rheumatic endocarditis became inactive, but there was a residual mitral incompetence.

The B.S.R. (Wintrobe) lengthened from 47.0 mm. a few days after the course of injections had been started, to 10.0 (Westergren) 5 months later.

The patient was discharged during the 26th week after admission, but was readmitted for mitral incompetence with tachycardia some 6 weeks later. He was redischarged after 5 months hospitalisation.
Febrile Reactions: Average duration $6\frac{1}{2}$ hours.
1st phase $3\frac{1}{2}$ hours; 2nd phase 5 hours.
Highest temperature attained - 103.0°F.
Average temperature peak - 101.9°F.
Fastest pulse-rate 160 per minute.

CASE 23.

Male, aged 11.

Family History: nil relevant.

Past History: Chorea at age of 9.

Onset of Present Chorea: 7 weeks before admission.
  Symptoms improved considerably, then
  an exacerbation occurred about a week ago.

Examination: Severe degree of chorea; more pronounced on the right side.
  General condition fairly good.
  Pulse-rate 94 per minute.
  Temperature 99.0°F.
  Heart: N.A.D.

Treatment: Patient isolated.
  Pyrifer injections commenced 2 days after admission; 7 given.

Progress: Little improvement shown till after the 4th reaction. After the 7th, symptoms were relatively mild, but they did not abate/
abate entirely until after another 30 days.
The B.S.R. (Wintrobe) was 62.0 mm. just after the commencement of the pyrifer injections; it lengthened to 7.0 mm. 5 months later. The patient was discharged during the 26th week after admission. No recurrence of symptoms within 9 months.

Febrile Reactions: Average duration 5\(\frac{1}{2}\) hours.
1st phase 2 hours; 2nd phase 3\(\frac{1}{2}\) hours. Highest temperature attained - 104.6\(^{\circ}\)F. Average temperature peak - 103.5\(^{\circ}\)F. Fastest pulse-rate 164 per minute.

**CASE 24.**

Female, aged 9.
Family history of rheumatism.
Past History: nil relevant.
Onset of Chorea: 2 weeks before admission.
Scarlet fever 6 weeks before.
Examination: Severe degree of chorea; generalised.
General condition good.
Pulse-rate 90 per minute.
Temperature 97.8\(^{\circ}\)F.
Heart; N.A.D.
B.S.R. (Micro-method) 20.0 mm.
Treatment: Patient isolated.

Pyrifer injections commenced on the day after admission; 5 given.

Progress: Symptoms mild after the 5th reaction, but did not disappear until the lapse of a further 36 days.

The B.S.R. shortened to 32.0 mm. just after the pyrifer injections then increased to 1.5 mm. a month later.

The patient was discharged during the 21st week after her admission.

No recurrence of symptoms within 8 - 9 months.

Febrile Reactions: Average duration 5½ hours.

1st phase 2½ hours; 2nd phase 3 hours.

Highest temperature attained - 103.6°F.

Average temperature peak - 102.6°F.

Fastest pulse-rate 128 per minute.

CASE 25.

Male, aged 11.

Family History: nil relevant.

Past History: Chorea when aged 8.

Onset of Present Chorea: 5 weeks before admission.

Symptoms getting worse latterly.

Examination: Severe degree of chorea; generalised.

General condition fairly good.
Cerebration rather sluggish.
Pulse-rate 100 per minute.
Temperature 96.4°F.
Heart: N.A.D.
B.S.R. (Westergren) 6.0 mm.

Treatment: Patient isolated.

Pyrifer injections commenced on the day after admission; 6 given.

Progress: Symptoms cleared up 18 days after the first reaction; 4 days after the last one. The patient was discharged 13 weeks after admission. No recurrence of symptoms within 8½ months.

Febrile Reactions: Average duration 5 hours.

1st phase 2 hours; 2nd phase 3 hours.

Highest temperature attained - 103.2°F.
Average temperature peak - 102.3°F.
Fastest pulse-rate 160 per minute.
GROUP 1 - MILD CASES.

A. ACUTE.

CASE 1.

Female, aged 12.
Family history of rheumatism.
Past History: nil relevant.

Onset of Chorea: 1 week before admission, ushered in by flitting joint pains of 1 week's duration. These subsided a few days ago with the advancement of the choreic symptoms.

Examination: Fairly mild degree of chorea; generalised.

- Pulse-rate 96 per minute.
- Temperature 97.0°F.
- Heart enlarged. Systolic and early diastolic aortic murmurs present.
- No pulsus celer. No capillary pulsation.
- B.S.R. (Cutler) 20 mm.

Treatment: Nirvanol gr.5 daily for 10 days.

Progress: Toxic rash appeared on the eleventh day, and/
and considerable improvement was noted thereafter. Slight symptoms persisted however until the 80th day. The patient was kept in hospital for just over another 12 months on account of the cardiac condition. The enlargement was reduced, but the to-and-fro murmur remained much the same. The B.S.R. lengthened to 13.0 mm. No reply was received to an enquiry re her health 18 months after being discharged.

CASE 2.

Female, aged 10.
Family History: nil relevant.
Past History: nil relevant.
Onset of Chorea: 2 weeks before admission.
Examination: Mild degree of chorea; generalised.
    Pulse-rate 104 per minute.
    Temperature 97.0°F.
    Heart enlarged. Mitral systolic murmur present, conducted to other cardiac areas and into the left axilla.
    B.S.R. (Cutler) 13.0 mm.
Treatment: Ca. aspirin gr.15 t.d.s.
Progress: Symptoms relieved 57 days after admission.
The apical systolic bruit persisted, but it was less audible.
The B.S.R. lengthened to 7.0 mm. after 4 months in hospital.
The patient was discharged 33 weeks after admission. No recurrence of symptoms within 2 years.

CASE 3.

Male, aged 13.

Family History: nil relevant.

Past History: Chorea 1 ½ years ago, preceded by flitting joint pains; a second attack occurred shortly afterwards.

Onset of Present Chorea: 2 months before admission.

Examination: Mild degree of chorea; generalised.

Pulse-rate 80 per minute.

Temperature 97.0° F.

Heart slightly enlarged. Systolic bruit in the pulmonary area; no accentuation of the 2nd sound.

B.S.R. (Cutler) 5.0 mm.

Treatment: Nirvanol gr.5 daily; discontinued after 14 days. No rash appeared.

Pot. bromid. gr.10 t.d.s. then exhibited.

Progress: Definite improvement noted after the nirvanol,
nirvanol, even in the absence of a toxic reaction, but occasional slight symptoms persisted until the 167th day after admission. Furunculosis troublesome during part of this period. Paronychia also had to be treated. The patient was discharged during the 28th week after admission. No recurrence of symptoms within 16½ months, although one attack of acute rheumatism was experienced.

B. SUBACUTE.

CASE 4.
Female, aged 10.
Family History: nil relevant.
Past History: nil relevant.
Onset of Chorea: 4 weeks before admission, with loss of the use of the left arm.
Examination: Mild degree of chorea, affecting the left side of body.
Pulse-rate 102 per minute.
Temperature 97·4°F.
Heart: N.A.D.
B.S.R. (Cutler) 4·0 mm.
White blood count = 8,080; granulocytes 4606/
4606 and lymphocytes 2748.

Treatment: Antipyrin gr.10 t.d.s.

Progress: Patient cured clinically 21 days after admission. A tachycardia in the region of 100 per minute persisted in spite of adequate rest in bed, and a very faint late systolic mitral murmur became audible 4 months after admission; it was strictly localised. The B.S.R. shortened to 7.5 mm., and lengthened again to 5.0 mm. within a further 3 months. The patient was discharged 22 - 23 months after admission. No recurrence of symptoms within just over 3 years.

CASE 5.

Female, aged 12.

Family history of rheumatism.

Past History: Tonsillectomy when aged 9.

Onset of Chorea: 4 weeks before admission. The symptoms had improved slightly when an attack of acute rheumatism supervened, and the patient was sent here.

Examination: Chorea fairly mild in degree; generalised. Pulse-rate 88 per minute.
Temperature 97·0°F.
Both ankles swollen and painful.
Heart not enlarged; no bruits.
B.S.R. (Cutler) 13·0 mm.
White blood count 9,000; 5,040 granulocytes and 3,330 lymphocytes.

Treatment: NIRVANOL GR. 5 daily until the toxic rash appeared on the 9th day.

Progress: With the appearance of the rash, the symptoms of chorea diminished considerably. The pain and swelling of the joints, which had flitted from the ankles to the knees a few days after admission, also abated. Signs of chorea not entirely absent however, until the lapse of another 50 days. The B.S.R. 5 months after admission was still 13·5 mm., but thereafter it gradually returned to normal.
The patient was discharged 27-28 weeks after admission.
No reply was received to an enquiry re her health 20 months later.
CASE 6.

Male, aged 5.

Family history of tuberculosis.

Past History: Broncho-pneumonia (post morbilli) at age of 2. Perennial attacks of asthma ever since.

Onset of Chorea: 10 weeks before admission.

Examination: Very mild degree of chorea; generalised.
  Pulse-rate 100 per minute.
  Temperature 97.6°F.
  Faint mitral systolic murmur. No accentuation of the pulmonary 2nd sound.
  Heart not enlarged. Lungs: N.A.D.
  B.S.R. not recorded.

Treatment: Sod. salicyl. gr.15 and Ca.lactate gr.15 t.d.s.

Progress: Symptoms relieved 14 days after admission.
  The murmur was inaudible 5 months later.
  The patient was discharged during the 22nd week after admission. Soon after his return home, mild symptoms of chorea reappeared, and have been present for over a year, according to a letter from his mother. She states that her son worries at school, and that her house is damp.
CASE 7.

Male, aged 7.

Family History: nil relevant.

Past History: Broncho-pneumonia (post pertussis) at age of 2.

Onset of Chorea: 7 weeks before admission.

Examination: Mild degree of chorea; generalised.

- Pulse-rate 78 per minute.
- Temperature 98.0°F.
- Heart: N.A.D. Lungs: N.A.D.
- B.S.R. not recorded.

Treatment: Patient isolated.

- Aspirin gr.10 q.d.s. and Ca.lactate gr.15 t.d.s.

Progress: Symptoms relieved 27 days after admission.

- The patient was discharged some 18 weeks later. 4 months later there was a recurrence of mild symptoms which lasted for 3 months.

CASE 8.

Female, aged 12.

Family History: nil relevant.

Past History: Tonsillectomy at age of 3.

- Several attacks of chorea during the past 3 years.
Onset of Present Chorea: 16 weeks before admission, preceded by a sore throat.

Examination: Very mild degree of chorea; generalised.
- Pulse-rate 84 per minute.
- Temperature 97.0°F.
- Heart enlarged. Systolic murmur present, loudest in the pulmonary area; pulmonary 2nd sound accentuated.
- B.S.R. (Cutler) 2.5 mm.

Treatment: Nirvanol gr.5 daily until rash appeared on the 11th day. Ca.lactate gr.20 t.d.s. also given.

Progress: Symptoms relieved 12 days after admission.
- Heart normal after 2 months' convalescence. The patient was discharged 19 weeks after admission. No recurrence of symptoms within 23 months.

CASE 9.

Male, aged 11.

Family History: Mother insane and died of 'gangrene of the lungs'.

Past History: nil relevant.

Onset of Chorea: 5 weeks before admission, after a sore throat.

Examination: Mild degree of chorea; generalised.
- Pulse-rate 76 per minute.
- Temperature 97.2°F.
Heart slightly enlarged; no bruits.
B.S.R. (Cutler) 8.0 mm.

Treatment: Nirvanol gr.5 daily for 9 days.

Progress: Improvement after the appearance of the toxic rash very slight. Symptoms finally disappeared 151 days after admission. Size of heart soon returned to normal. The patient was discharged during the 27th week after admission. No recurrence of symptoms within 17 months.

CASE 10.

Female, aged 9.

Family: nil relevant.
Past History: nil relevant.
Onset of Chorea: 6 weeks before admission.

Examination: Very mild degree of chorea, affecting the left side only.
Pulse-rate 88 per minute.
Temperature 97.4°F.
Heart: N.A.D.
B.S.R. (Micro-method) 8.0 mm.

Treatment: Aspirin gr.10 and Ca.lactate gr.15 q.d.s.

Progress: Symptoms relieved 79 days after admission. The patient was discharged during the 25th week after admission. No recurrence of symptoms within 18½ months.
CASE 11.

Female, aged 5.
Family History: nil relevant.
Past History: nil relevant.
Onset of Chorea: 4 weeks before admission.
Examination: Mild degree of chorea, affecting the left side especially.
Pulse-rate 96 per minute.
Temperature 97.6°F.
Heart: N.A.D.
B.S.R. (Cutler) 5.0 mm.

Treatment: Nirvanol gr.5 daily until appearance of toxic rash after 9 days.
Progress: Symptoms very slight after nirvanol, but did not disappear for a further 34 days.
A systolic apical bruit appeared 7 months after admission. The patient was discharged about 5 months later with no obvious cardiac disturbance. No recurrence of symptoms within 19 months.

CASE 12.

Female, aged 9.
Family History: nil relevant.
Past History: nil relevant.
Onset of Chorea: 3 weeks before admission.

Examination: Mild degree of chorea; generalised.
- Pulse-rate 80 per minute.
- Temperature 97.8°F.
- Systolic bruit in pulmonary area; no accentuation of the 2nd sound. Heart not enlarged.
- B.S.R. (Micro-method) 4.0 mm.

Treatment: Merely rest in bed.

Progress: Symptoms relieved 61 days after admission.
The patient was discharged 6 weeks later, but was readmitted within 3 months suffering from an attack of acute rheumatism. No recurrence of chorea.

CASE 13.

Male, aged 9.

Family history of rheumatism.

Past History: nil relevant.

Onset of Chorea: 6 weeks before admission, preceded for 2 months by 'growing pains'.

Examination: Mild degree of chorea; generalised.
- Pulse-rate 88 per minute.
- Temperature 97.0°F.
- Heart enlarged; apical systolic bruit present.
- B.S.R. not recorded.
Treatment: Patient isolated.

Ca. aspirin gr. 10 b.i.d. and adexolin liq. m.10 b.i.d. exhibited.

Progress: Symptoms relieved 26 days after admission. Heart normal within a further month.

The patient was discharged during the 11th week after admission. No recurrence of choreic symptoms within 15 months, but an attack of acute rheumatism occurred 10 months or so after his return home.

CASE 14.

Male, aged 6.

Family History: nil relevant.

Past History: Tonsillectomy at age of 2.

Acute rheumatism 13 months ago.

Rheumatic endocarditis 5 months ago.

Onset of Chorea: 8 weeks before admission.

Examination: Mild degree of chorea; bilateral, but the legs were unaffected.

Pulse-rate 102 per minute.

Temperature 97.0°F.

Heart: N.A.D.

White blood count 7,100; lymphocytes 5,112.

B.S.R. (Wintrobe) 1.0 mm.
Treatment: Ca. aspirin gr.10 t.d.s.

Progress: Symptoms relieved 21 days after admission. A systolic bruit became audible in the pulmonary area about a week after admission; it disappeared however, within a further month.

The patient was discharged 9 weeks after admission. No recurrence of symptoms within 7 - 8 months.

C. CHRONIC.

CASE 15.

Female, aged 12.

Family History: nil relevant.

Past History: nil relevant.

Onset of Chorea: 28/12 years before admission, preceded for 2 months by 'growing pains'. Symptoms generally of a very mild character with occasional slight exacerbations.

Examination: Very mild degree of chorea; generalised. Pulse-rate 96 per minute. Temperature 98.0°F. Heart: N.A.D.

B.S.R. (Micro-method) 14.0 mm.
Treatment: Aspirin gr. 20 t.d.s. and Ca. lactate gr. 30 t.d.s.

Progress: Symptoms disappeared 120 days after admission. The B.S.R. fell to 6.5 mm. (Cutler) within 3 months. The patient was discharged 20 - 21 weeks after admission. No recurrence of symptoms within 12 months.

GROUP 2 - MODERATE CASES.

A. ACUTE.

CASE 16.

Male, aged 12.

Family History: nil relevant.

Past History: Acute rheumatism and chorea 5 years ago.

Onset of Present Chorea: 1 week before admission, immediately following an attack of acute rheumatism.

Examination: Moderately severe degree of chorea.

Pulse-rate 80 per minute.

Temperature 97.0°F.

Heart enlarged. Systolic mitral murmur, propagated/
propagated into left axilla; pulmonary 2nd sound accentuated.
B.S.R. (Cutler) 12.0 mm.

Treatment : Nirvanol gr.5 daily for 5 days.
Progress : Pyrexia occurred on the 5th day with aggravation of the chorea and of the endocarditis. Considerable lessening of the movements was however noted after the appearance of the toxic rash on the 5th day. The temperature remained high for a few days, during which time the B.S.R. rose to 29.5 mm., then it fell to just above normal for another 30 days before remitting. The B.S.R. returned to normal (5.0 mm.) within 3 months, but mild choreic symptoms persisted for 102 days, and the cardiac symptoms took considerably longer to return to their pre-nirvanol status. Ca.aspirin gr.15 q.d.s. was exhibited during the period of active infection. The patient was discharged during the 29th week after admission. No recurrence of symptoms within 22 months.
CASE 17,

Female, aged 7.

Family history of rheumatism.

Past History: Tonsillectomy when aged 4½.

Onset of Chorea: 6 weeks before admission, associated with an attack of acute rheumatism which lasted for 12 days.

Examination: Moderately severe degree of chorea; generalised.
Pulse-rate 100 per minute.
Temperature 97.2°F.
Heart enlarged. Systolic mitral bruit, propagated into the left axilla.
Pulmonary 2nd sound accentuated.
B.S.R. (Cutler) 5.0 mm.

Treatment: Nirvanol gr.5 daily given to toxicity; 11 days.

Progress: Improvement during the first 2 months only slight. Ca.lactate gr.15 t.d.s. then exhibited. Symptoms began to diminish slowly and disappeared 112 days after admission. Heart signs also cleared up entirely after a further 10 months and the patient was discharged in apparent perfect health. 45-46 weeks after admission.
There was a recurrence of the chorea 3 months later however, the attack lasting about 2 months.

CASE 15.

Female, aged 10.

Family history of rheumatism.

Past History: Chorea at age of 7.

Onset of Present Chorea: 5 weeks before admission.

Symptoms mild to begin with; getting worse latterly.

Examination: Moderately severe degree of chorea; generalised.

Pulse-rate 94 per minute.

Temperature 97.0°F.

Heart: N.A.D.

B.S.R. not recorded.

White blood count 8,080; granulocytes 5,010 and lymphocytes 2,909.

Treatment: Nirvanol gr.5 given daily for 4 days.

Progress: Considerable improvement noted after the appearance of the toxic rash on the 5th day. Muscular hypotonia and occasional slight movements persisted however for a further period of 67 days. Tachycardia still present nevertheless, and patient kept in bed. A diffuse swelling/
swelling of the thyroid became evident about a month later.
The patient was discharged 41 - 42 weeks after admission.
No recurrence of symptoms within 2 years.

CASE 19.

Male, aged 7.

Family History: nil relevant.

Past History: Asthma perenially since early childhood. Tonsillectomy at age of 5.

Whooping-cough 7 months ago.

Onset of Chorea: 5 weeks before admission, preceded by 'growing pains'.

Examination: Moderately severe degree of chorea; generalised.

Pulse-rate 88 per minute.

Temperature 98.4°F.

Systolic murmur in the pulmonary area; no accentuation of the 2nd sound.

Heart not enlarged.

B.S.R. (Cutler) 2.5 mm.

Treatment: Nirvanol gr.5 daily for 14 days; no reaction.

Progress: In spite of the absence of a reaction, moderate improvement was noted.
Ca. aspirin gr. 10 t.d.s. exhibited 2 months later owing to the persistence of mild symptoms. These did not entirely disappear until the 150th day after admission. A faint bruit persisted in the pulmonary area. The patient was discharged 24 weeks after admission. No reply to an enquiry re his health 15 months later.

CASE 20.

Female, aged 22.

Family history both of rheumatism and of tuberculosis.

Past History: Acute rheumatism at the age of 12.

'Nervous breakdown' during early adolescence.

Onset of Chorea: 6 weeks before admission.

Examination: Moderately severe degree of chorea, affecting the left side of the body only. Pulse-rate 102 per minute.

Temperature 97.2°F.

One very carious tooth.

Heart: N.A.D.

B.S.R. (Micro-method) 4.5 mm.

Treatment: Aspirin gr. 10 t.d.s.

Progress: After 45 days' treatment only a slight improvement/
improvement shown, but patient discharged at her own request. She was re-admitted 66 days later with an attack of erythema nodosum; chorea unaltered. Pot. bromid. gr. 10 and liq. arsenicalis m. 5 given t.d.s. The skin condition cleared up within a week or so. The chorea took 57 days to clear up, improvement being more rapid following an attack of follicular tonsillitis 1 month after readmission.

She was discharged 5 weeks later.

No reply received to an enquiry re her health 15 months afterwards.

CASE 21.

Female, aged 9.

Family History of rheumatism.

Past History: Jaundice (? origin) when aged 6.

chorea 6 months ago.

Onset of Present Chorea: 3 weeks before admission.

Examination: Chorea moderately severe; generalised.

Pulse-rate 96 per minute.

Temperature 98.0°F.

Heart: N.A.D.

B.S.R. (Micro-method) 8.0 mm.
Treatment: Aspirin gr.20 and calcium lactate gr.30 given t.d.s.

Progress: Clinical cure 105 days after admission.
The B.S.R. had now lengthened to 4.0 mm.
The patient was discharged during the 24th week after admission.
There was a recurrence of symptoms just under a year later.

CASE 22.

Female, aged 13.
Family History of rheumatism and chorea.
Past History: Scarlet fever at age of 9.
Tonsillitis 6 months ago, followed by 'growing pains' which lasted for almost 6 months.
Onset of Chorea: 3 weeks before admission, shortly after the cessation of the growing pains.
Examination: Chorea moderately severe; more pronounced on the right side.
Several decayed teeth.
Heart: N.A.D. B.P.144/82.
No urinary abnormality. Fundi normal.
B.S.R. (Micro-method) 14.0 mm.
Treatment: Nirvanol gr.5 daily for 12 days; no rash appeared. Aspirin gr.15 and Ca. lactate/
lactate gr. 20 t.d.s. then exhibited.

Progress: Symptoms unaltered after the nirvanol in the absence of a toxic reaction. Gradual improvement noted a week or two after the substitution of calcium and aspirin. Patient clinically cured 98 days after admission. The B.S.R. fell to 8.0 mm. She was discharged during the 20th week after admission. No recurrence of symptoms within 14 months.

CASE 23.

Female, aged 8.

Family History: nil relevant.

Past History: Scarlet fever when aged 4; radical mastoid operation the same year. Frequent attacks of coryza since.

Onset of Chorea: 9 weeks before admission.

Examination: Moderately severe degree of chorea, affecting the right side only.

Pulse-rate 92 per minute.

Temperature 97.6°F.

Heart not enlarged. Systolic murmur in pulmonary area; no accentuation of the 2nd sound.

B.S.R. (Micro-method) 27.0 mm.
Treatment : Ca.aspirin gr.15 t.d.s.

Progress : Symptoms relieved 132 days after admission. The bruit disappeared. The B.S.R. lengthened to 2'0 mm. The patient was discharged 29 weeks after admission. No recurrence of symptoms within 13 months.

GROUP 3 - SEVERE CASES.

A. ACUTE.

CASE 24.

Female, aged 12.

Family History of rheumatism.

Past History : Acute rheumatism at the ages of 5 and 11. Tonsillectomy when aged 9.

Onset of Chorea : During convalescence in this hospital, 11 months after admission for a further attack of rheumatic fever.

Examination : Severe degree of chorea; generalised. Pulse-rate 94 per minute. Temperature 98.0°F. Both aortic and mitral incompetence present as an aftermath of the rheumatic fever.
B.S.R. not recorded.

Treatment: Nirvanol gr.5 daily for 11 days.

Progress: Toxic rash appeared on the 12th day. Considerable improvement noted thereafter, and movements were practically gone by the 25th day. No symptoms after 53 days. There was no evidence of an exacerbation of the rheumatic endocarditis, the cardiac symptoms being aggravated only to a degree commensurate with the extra strain thrown upon the heart by the gross movements. The patient was discharged some 18 months after admission, but was readmitted 9 months later with congestive cardiac failure. She died within 3 months.

CASE 25.

Female, aged 12.

Family history of rheumatism.

Past History: Acute rheumatism 1 month before admission.

Onset of Chorea: 2 weeks ago.

Examination: Severe degree of chorea; generalised. Pulse-rate 86 per minute. Temperature 97.0°F. Heart slightly enlarged. Mitral systolic murmur present, propagated to the other cardiac/
cardiac areas and into the left axilla. Accentuation of the pulmonary 2nd sound. B.S.R. (Cutler) 17.0 mm. White blood count 8,300; granulocytes 5,810 and lymphocytes 1,826.

**Treatment** : Nirvanol gr. 5 given daily for 5 days.

**Progress** : Considerable improvement noted after the appearance of the toxic rash on the 6th day. Symptoms became worse again 3 weeks later, but after a short stationary period, they gradually diminished, to disappear on the 106th day after admission. A short mitral systolic murmur persisted, but the cardiac response to effort was good. The patient was discharged 30 - 31 weeks after admission. No recurrence of symptoms within 23 months.
THERAPEUTIC RESULTS.

The therapeutic results are summarised in the following 4 tables.

<table>
<thead>
<tr>
<th>TABLE 1.</th>
<th>AVERAGE DURATION OF THE ATTACK.</th>
</tr>
</thead>
<tbody>
<tr>
<td>TYPE</td>
<td>NO. of CASES.</td>
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<tr>
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<td>(b) Subacute</td>
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<tr>
<td>(c) Chronic</td>
<td>2</td>
</tr>
<tr>
<td>Control</td>
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<td>(a) Acute</td>
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<td>(b) Subacute</td>
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<td>(b) Subacute</td>
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<tr>
<td>(c) Chronic</td>
<td>2</td>
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<tr>
<td>Control</td>
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<tr>
<td>(a) Acute</td>
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<tr>
<td>(c) Chronic</td>
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<td>Control</td>
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<tr>
<td>(a) Acute</td>
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<tr>
<td>(c) Chronic</td>
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TABLE 1 (cont.).

<table>
<thead>
<tr>
<th>TYPE</th>
<th>No. of CASES</th>
<th>AVERAGE DURATION in DAYS</th>
<th>RANGE in DAYS</th>
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<tbody>
<tr>
<td>ACUTE</td>
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TABLE 2.

AVERAGE NUMBER OF REACTIONS FOUND NECESSARY.

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<th>TYPE</th>
<th>Acute</th>
<th>Subacute</th>
<th>Chronic</th>
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<td>Mild</td>
<td>4.83</td>
<td>7.00</td>
<td>5.33</td>
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<tr>
<td>Moderate</td>
<td>5.70</td>
<td>4.00</td>
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<tr>
<td>Severe</td>
<td>6.78</td>
<td>6.50</td>
<td>6.86</td>
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The average number of pyrifer injections given in the whole series was 5.88 (range 2 - 12).
### TABLE 3.

**RELEATION OF THE AVERAGE DURATION OF THE ATTACK TO THE AVERAGE HEIGHT OF THE PYREXIA ATTAINED.**

<table>
<thead>
<tr>
<th>TYPE</th>
<th>No. of CASES</th>
<th>FASTIGIUM below 102°F</th>
<th>FASTIGIUM 102-103°F</th>
<th>FASTIGIUM over 103°F</th>
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<td><strong>MILD</strong></td>
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<td>(a) Acute</td>
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<td>(c) Chronic</td>
<td>2</td>
<td>-</td>
<td>45</td>
<td>-</td>
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<tr>
<td><strong>MODERATE</strong></td>
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<td>(a) Acute</td>
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<td>14</td>
<td>-</td>
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<td>(b) Subacute</td>
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<td>55</td>
<td>29</td>
<td>38</td>
</tr>
<tr>
<td>(c) Chronic</td>
<td>2</td>
<td>-</td>
<td>46</td>
<td>-</td>
</tr>
<tr>
<td><strong>SEVERE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Acute</td>
<td>2</td>
<td>-</td>
<td>7</td>
<td>23</td>
</tr>
<tr>
<td>(b) Subacute</td>
<td>7</td>
<td>25</td>
<td>34</td>
<td>47</td>
</tr>
<tr>
<td>(c) Chronic</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>ACUTE</strong></td>
<td></td>
<td>19</td>
<td>7</td>
<td>23</td>
</tr>
<tr>
<td><strong>SUBACUTE</strong></td>
<td></td>
<td>29</td>
<td>29</td>
<td>42</td>
</tr>
<tr>
<td><strong>CHRONIC</strong></td>
<td></td>
<td>46</td>
<td>45</td>
<td>-</td>
</tr>
</tbody>
</table>

The average fastigium reached in the total series was 102.3°F.
### TABLE 4.

**RELATION OF THE AVERAGE DURATION OF THE ATTACK TO THE AVERAGE DURATION OF THE PYREXIA.**

<table>
<thead>
<tr>
<th>TYPE</th>
<th>No. of CASES</th>
<th>PYREXIA of 3-4 HOURS</th>
<th>PYREXIA of 4½-5½ HOURS</th>
<th>PYREXIA of 6-8½ HOURS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MILD</strong></td>
<td>6</td>
<td>34</td>
<td>21</td>
<td>23</td>
</tr>
<tr>
<td>(a) Acute</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>23</td>
</tr>
<tr>
<td>(b) Subacute</td>
<td>3</td>
<td>14</td>
<td>21</td>
<td>-</td>
</tr>
<tr>
<td>(c) Chronic</td>
<td>2</td>
<td>45</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>MODERATE</strong></td>
<td>10</td>
<td>29</td>
<td>34</td>
<td>70</td>
</tr>
<tr>
<td>(a) Acute</td>
<td>1</td>
<td>14</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>(b) Subacute</td>
<td>7</td>
<td>39</td>
<td>34</td>
<td>-</td>
</tr>
<tr>
<td>(c) Chronic</td>
<td>2</td>
<td>22</td>
<td>-</td>
<td>70</td>
</tr>
<tr>
<td><strong>SEVERE</strong></td>
<td>9</td>
<td>-</td>
<td>35</td>
<td>29</td>
</tr>
<tr>
<td>(a) Acute</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>15</td>
</tr>
<tr>
<td>(b) Subacute</td>
<td>7</td>
<td>-</td>
<td>35</td>
<td>36</td>
</tr>
<tr>
<td>(c) Chronic</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>ACUTE</strong></td>
<td>4</td>
<td>14</td>
<td>-</td>
<td>18</td>
</tr>
<tr>
<td><strong>SUBACUTE</strong></td>
<td>17</td>
<td>31</td>
<td>31</td>
<td>36</td>
</tr>
<tr>
<td><strong>CHRONIC</strong></td>
<td>4</td>
<td>37</td>
<td>-</td>
<td>70</td>
</tr>
</tbody>
</table>

In the total series, the average duration of the pyrexia produced was 5½ hours (range 1-17½), the 1st phase occupying 2½ hours (range½-4½) and the 2nd phase 3 hours (range ½-6½).
UNUSUAL REACTIONS.

No unusual reactions occurred in this series of cases, if the very occasional occurrence of severe peripheral circulatory embarrassment during the rigor, necessitating the administration of adrenaline, be excluded.

It was noted that the affected children in such cases exhibited enlarged tonsils.

Such a happy state of affairs, while usual, has not unfortunately been constantly experienced in the use of non-specific protein therapy. Thus Hench (1932) reports an incidence of 0.2% unusual reactions after 10,000 injections of T.A.B. vaccine, involving about 0.5% of 2,500 patients treated. They occurred 17 times in the treatment of 12 patients with arthritis (including one patient with rheumatic fever) and 3 times in the treatment of 2 patients with occlusive vascular disease. He listed them as follows:--

acute and subacute appendicitis, cholecystitis, enteritis, pleurisy, pericarditis, iritis, glaucoma, adenitis, extensive vascular thrombosis, and renal insufficiency.

Death occurred in 3 instances, a mortality rate of 0.12%. He has collected numerous reports of unusual reactions from the literature, including upwards of a score of fatalities, but goes on to say that careful selection of cases can possibly obviate the latter risk, slight as it is. It is difficult to see/
see how this ideal can be attained however, as he mentions over a dozen deaths due to "anaphylaxis". Hench's list of untoward results occurred, of course, in adults.

**RELAPSE RATE.**

A recent comprehensive enquiry revealed the following incidence of recurrences:

A. **PYRIFER SERIES OF CASES.**
   Followed up within 7-16\(\frac{1}{2}\) (average 11) months after the disappearance of symptoms.
   No reply received in 4 instances.
   Chorea recurred in 4 cases (19%).

B. **CONTROL SERIES OF CASES.**
   Followed up within 7 months - 3 years (average 18 months) after the disappearance of symptoms.
   No reply received in 4 instances.
   Chorea recurred in 4 cases (19%).

Other rheumatic manifestations had occurred in 9 of the 42 cases (21.43%).
DISCUSSION.

Numerous statistical studies on the successful use of non-specific protein therapy in various diseases, both acute and chronic, have been published. Most of them have been uncontrolled however, thereby rendering a true assessment of their therapeutic value difficult. Further, many of the often rather startling claims have been made with regard to certain chronic diseases such as multiple sclerosis and chronic arthritis, which are characterised by periodic remissions.

In the present series of 25 cases of Sydenham's chorea treated by pyrifer injections, there has been an attempt at careful control, admittedly not with cases treated by adequate rest only, but with cases receiving supplementary treatment by other accepted methods.

Of the total 50 cases, 29 were females and 21 were males, a ratio of 1.38 to 1, which is much lower than that of approximately 3 to 1 usually encountered.

The attacks were recurrent in 13 instances (26%).

The ages of the patients varied from 5 years to 22 years, the average being 10.30 years (females 10.86 and males 9.52). The age of mild cases averaged 9.60 years (females 10.15 and males 8.57), that of moderate cases 10.58 years (females 11.09 and males 9.88), and that of severe cases 11.09 years (females 12.20 and males 10.17).
If cases with recurrent attacks are excluded, then the average age was 10.11 years (females 10.77 and males 9.13), that of mild cases being 9.35 years (females 10.18 and males 7.63), of moderate cases 10.71 years (females 11.50 and males 9.67), and of severe cases 10.83 years (females 11.00 and males 10.67).

These findings are quite in keeping with the conception that attacks increase in severity with the proximity of puberty.

There was a family history of rheumatism in 13 cases (26%), including chorea in 2 instances (4%), and of tuberculosis in 5 cases (10%).

A personal history of rheumatism was elicited in 20 cases (40%), 15 having had rheumatic arthritis (30%) and 5 having experienced 'growing pains' (10%).

Six further cases (12%) gave a history of tonsillitis or 'sore throats'. Clinical evidence of cardiac involvement was found in 24 cases (48%), but in only 15 cases (30%) could the presence of actual active disease be definitely established, as judged by pyrexia, tachycardia, cardiac enlargement, suggestive bruits, accentuation of the pulmonary 2nd sound, rapid B.S.R., slow response to treatment, and impaired cardiac response to effort. Of these 15 cases only 5 (10%) did not exhibit any coincident stigmata of rheumatism (apart from the carditis).

Jones and Bland (1936) collected 452 cases of chorea and/
and found that 54% showed clinical signs of cardiac damage. They divided their cases into 2 groups, those with "pure" chorea and those with other coincident rheumatic manifestations. Only 3% of the former group had clinical heart disease, while 73% of the latter group showed it. This is a very artificial classification however, for who can be certain if or when chorea is "pure"?

The sedimentation rate of the blood was increased in 24 cases (63.16%). In 14 cases (36.84%) it was normal, while in the remaining 12 cases no readings were taken on admission.

With adequate rest, the spontaneous recovery rate in Sydenham's chorea approaches 100%. The value of the therapeutic results obtained is best assessed therefore in terms of the resultant shortening of the average duration of the attack. The incidence of untoward sequelae, the course of convalescence, and the relapse rate are additional points that require investigation.

There can be no question that pyrifer therapy, in common with other non-specific protein methods, definitely lessens the severity of the attack. The average duration of the attack was shortened from 77.44 days in the control series to 31.84 days in the pyrifer series, a difference of 143%.

It might justifiably be pointed out that the pyrifer results/
results may not be accurate, as several of the cases were in hospital some time before the treatment was commenced, and had perhaps already improved to a certain extent. To meet this criticism, one can delete 4 cases (numbers 4, 5, 6, and 15) who were in hospital for over a fortnight before treatment was begun. The average duration of the attack in the remaining 21 cases is actually reduced to 29.10 days. While if one limits the series to those treated within a week of admission, deleting cases 8 and 9 also, the average duration in the 19 remaining cases is reduced still further to 28.21 days.

The mild attacks were shortened from 62.53 days to 28.00 days (123%), the moderate from 104.88 days to 35.20 days (193%), and the severe from 79.50 days to 30.67 days (159%).

Those treated in the acute stage were shortened from 95.50 days to 16.75 days (470%), those in the subacute stage from 69.01 days to 32.24 days (114%), and those in the chronic stage from 120.00 days to 45.25 days (165%).

There are unfortunately not a sufficient number of cases to enable one to satisfactorily evaluate the results in cases classified by combining the different degree of severity and chronicity.

Mild subacute, mild chronic, and moderate subacute attacks yielded less readily to treatment, the average duration/
duration being shortened 150% (46.73 days to 18.67), 170% (120.00 days to 44.50 days), and 196% (104.14 days to 35.14 days) respectively. On the other hand, moderate acute, severe acute, and mild acute attacks were much more susceptible to treatment, the average duration being reduced by 666% (110.00 days to 14.00 days), 430% (79.50 days to 15.00 days), and 341% (101.33 days to 23.00 days) respectively. It is impossible to directly compare these figures with those obtained by other workers, not the least difficulty being the different individual criteria set as to when the disease can be considered cured. This difficulty could be largely overcome if every series of cases were carefully controlled. Sutton and Dodge (1936) are apparently the only authors to have adequately done so. They were able to shorten the duration of the attack from 42.60 days in a control series of 150 cases, to 3.5 days in a series of 150 cases treated by an average of 6.24 daily injections of graduated doses of T.A.B. vaccine, a remarkable reduction of 401%. Mild attacks were shortened from 27.40 days to 5.72 days (379%), those of moderate severity from 44.00 days to 3.56 days (414%), and severe attacks from 62.40 days to 15.80 days (295%). Superficially, at least, these results are amazingly good. No indication is given however of the chronicity of the chorea before treatment was started. The authors...
authors were fortunate enough to find that their mild cases all yielded rapidly to treatment, difficulty being only experienced in the severe types. Thus the longest duration of a mild attack was 14 days, of a moderate attack 22 days, and of a severe attack 47 days.

This has not been the writer's experience. Refractory cases were encountered in all 3 groups, the longest duration of a mild attack being 70 days, of a moderate attack 70 days, and of a severe attack 54 days. Incidentally Ash and Einhorn (1935) found that cases with the most marked movements showed the most rapid improvement with the T.A.B. vaccine therapy, and that those with generalised movements improved more rapidly than did those in whom the movements were localised. Again, 45.33% of Sutton and Dodge's cases were mild and only 16.67% severe. On the other hand, in the present series only 24.00% were mild cases, while 36.00% were severe. In the former series too, daily reactions were induced, while in the latter series injections were given every 2nd day. While dramatic results are very gratifying, the question arises as to whether such rapidity of acquirement is really desirable when produced by such drastic means. After all, non-specific protein therapy is a very heroic method of treatment, taxing both the physical and mental resources of the patient. It is indeed a moot point whether patients should be/
be subjected to such a therapy as frequently even as every 2nd day. The writer has tried the administration of daily injections, but quickly abandoned the procedure, largely because of the undoubted strain thrown upon hearts whose functional ability is not infrequently suspected, or actually known to be already impaired, and, not in the least, because of the look of apprehension with which the affected children were wont to greet his appearance on the wards, except in those very severe cases of course, in whose faces it would be a nice point of discrimination to detect any form of emotional expression. Sutton and Dodge have again been fortunate in this respect, as their patients apparently began to actually look forward to their injections, realising that their illness would thereby be curtailed.

Most workers maintain that the higher the average temperature produced the better the result. Some of them go to very considerable trouble to gain this end, even to the length of administering supplementary doses of the vaccine or other protein agent used. Reference to Table 3 (p. 90) will show that the writer's figures do not support this contention. The best results were attained when the average height of the pyrexia lay between 102° - 103°F. The average fastigium tended to be higher in the more severe/
severe cases, and lower in the more chronic types. Reference to Table 4 reveals the fact that curtailment of the average duration of symptoms bore no definite relation to the average duration of the hyperthermia. Certainly the patients in whom the pyrexias lasted longest did not reap any corresponding benefit. The febrile reactions tended to be of longer duration in the severer types of chorea. In general, as one might expect, more injections were needed to produce the desired results in the severer cases.

There were no untoward sequelae. Incipient symptoms of vasomotor collapse were seen on one or two occasions, but they were invariably quickly relieved by the exhibition of adrenaline. Tonsillar enlargement was a constant, possibly fortuitous association in the few cases so affected. There may have been an element of the focal reaction present, although local pain was never experienced.

After certain modes of non-specific protein therapy, for example malaria therapy, patients are decidedly exhausted and anaemic, and require a considerable period of convalescence. This has not been the writer's experience with pyrifer, nor with T.A.B. vaccine for that matter, convalescence usually being uneventful. In chorea, of course, the general condition of the patient is seldom poor at the outset. The relapse rate in both series of cases was identical,
19%. This finding subscribes to the generally accepted view that recurrences are in fact associated with rheumatic reinfection. In this connection it is interesting to note that in 9 instances out of 42 replies (21.43%), other rheumatic manifestations had occurred. There is no suggestion that any associated endocarditis was ever aggravated either immediately or remotely by the pyrifer reactions. How may non-specific protein therapy produce its undoubtedly beneficial effect in chorea, and in other diseases? It is only by a thorough study of this question that the status of the remedy will be eventually raised above that of the empiricism in which it originated, like so many of our most useful therapeutic procedures nevertheless. There can be little doubt that the physiological effect of primary value is the dilatation of the capillaries that is produced, in association with an augmentation of their number and an increase in their permeability. This action is maintained by the generation of heat, and heat, we must remember, is the only known means of producing capillary dilatation for any reasonable length of time. The most important part of the circulatory system is that constituted by the capillaries, for it is these vessels that are most intimately concerned with the maintenance of cellular life. It is ultimately through them that the tissues are enabled to respire.
It is ultimately through them that specialised tissues are enabled to utilise specific substances essential for the continuance of their vital functions.

It is ultimately through them that damaged tissues can receive aid, and that other tissues can send out defensive substances or cells, perhaps often specific in nature, to help their stricken partners.

Various other potentially beneficial changes are also produced. Thus there is an increase of leucocytes, an actual increase, as is shown by the shift to the left in the Arneth count. There is an augmentation of circulating antibodies, complement, ferments, etc. Whether this increase is actual or relative, due to humoral mobilisation, is uncertain, but the probability is that both factors are concerned.

A further change that must be considered is the heightened temperature of the body. High temperatures are inimical to bacteria, especially if maintained for certain periods of time. It is improbable however that the comparatively moderate pyrexias sought by the therapeutic injection of proteins can have any action in this respect, for adequate temperatures would undoubtedly jeopardise the viability of the actual bodily cells.

Just which one or more of these additional physiological changes are operable in Sydenham's chorea it would be hazardous to say, as we do not fully understand the pathogenesis of the disease. It would seem/
that the facilitated access of blood, possessing enhanced bactericidal powers, to the general bodily tissues might well be the means of counteracting the rheumatic infection which is, directly or indirectly, causing an irritation of certain cerebral tissues. On this hypothesis, it is clear that an increase in the bactericidal power of the blood must vary considerably with the ability of the patient’s tissues to respond to stimulation. Thus it would be quite reasonable to simultaneously exhibit anti-rheumatic sera (e.g. antiscarlatinal) in refractory cases. The writer has never done so.

It can logically be concluded that non-specific protein therapy is a valuable addition to our present therapeutic armamentarium against Sydenham's chorea. The results obtained in the present series of cases suggest that it is most applicable to the more severe type of case, more especially if the attack is still in its acute stage. Furthermore, it seems rather unwarranted to subject mild cases to such an heroic remedy, unless they are resistant to other methods of treatment. One must remember too, that chronic cases often have a large functional element superimposed upon the organic basis. There would appear to be no necessity to strive for high pyrexias of long duration, a febrile reaction of 4 - 6 hours, showing a maximum temperature of 102°F - 103°F., being apparently ample. It is doubtful if reactions can be induced, without/
without causing some harm, oftener than every 2nd day, even this rate of frequency being perhaps too great, in cases with cardiac involvement at least. The intravenous injection of a B. coli vaccine, sold under the name of "pyrifer", is a reliable means of producing a satisfactory protein reaction. It is a comparatively cheap remedy. The first 4 strengths cost approximately 1/- each, the succeeding 2 strengths approximately 1/6d. each, and strength 7 2/-. Thus the usual average of 6 injections entail an expense of about 7/-. This is much less (nearly 150%) than the cost of an equivalent number of T.A.B. vaccine injections.

It is the phase associated with the rigor that is so distressing to the patients, and everything should be done to make them comfortable during this period. It remains to be seen, whether the recent claims made with regard to the success of pyretotherapy produced by physical methods can be substantiated. The treatment certainly seems to be much less exacting than intravenous protein therapy, and the height and duration of the pyrexias are apparently more easily controlled. The writer has never experienced any great difficulty in the latter respect with pyrifer. If necessary, pyrexias produced by protein therapy could in fact be maintained in air-conditioned cabinets or "treatment bags" such as American authors describe.
The question naturally arises as to whether heat applied externally will prove to be as efficacious as heat generated internally. Pyrexia produced by means of electromagnetic induction by high frequency currents is said to be of internal origin.

**SUMMARY AND CONCLUSIONS.**

1. Non-specific protein therapy, intravenously administered, although an heroic measure, is a valuable remedy for Sydenham's chorea in the present state of therapeutic knowledge.

2. Its beneficial effect is possibly obtained through an enhancement of the bactericidal powers of the body, with an eventual overwhelming of the rheumatic infection which has been proving a source of irritation, direct or indirect, to certain of the cerebral tissues.

3. The method was successfully employed in a series of 25 cases. These have been carefully controlled by a further series of 25 cases treated by other accepted methods.

4. "Fyrifer", a B. coli vaccine, provides a comparatively cheap, safe, and reliable means of producing satisfactory protein reactions.

5. Heart disease, if adequately compensated, does not contraindicate the use of this mode of therapy.

6. Constant expert supervision, preferably in an institution,
institution, is essential.

7. Better results are obtained if treatment can be inaugurated during the early stages of an attack.

8. This drastic therapeutic procedure is uncalled for in the milder types of chorea, unless they have proved refractory to other remedies.

9. Febrile reactions of 4 - 6 hours, showing a temperature peak of 102° - 103°F., were the most effective.

10. The relapse rate was unaffected.

I am indebted to Dr. E. C. Hadley, medical superintendent of the City General Hospital, Leicester, for permission to make free use of the case notes.
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