THE CATARRHAL STATE

P. D. Mulkern, M.R.C.S., L.R.C.P.
Romford

It was during the measles epidemic of the autumn of 1951 to the spring of 1952 that I blundered—for there is no other more suitable word to describe my shameful and unscientific empiricism—on a useful treatment to control the catarrhal state. Frequent upper respiratory tract infections, otorrhoea, sinusitis and tonsillitis became the accepted accompaniment of convalescence from measles in this working-class practice. Quite a number of adults were known to have quiescent tuberculosis and I was anxious that children debilitated by measles should not inadvertently become infected by neighbours as they played in other houses. So it became a routine to use the jelly test for tuberculin sensitivity during the 6 months after recovery in any children who appeared to be unduly debilitated, prone to frequent colds and catarrh, or who suffered multiple attacks of upper respiratory tract infection of one kind or another. I found quite a number of positive reactors, although on looking round I could never trace the source. Nor could I detect any physical signs of a primary focus by clinical or radiological examinations. Nevertheless, I decided to try the effect of rimifon on these children who were underweight, full of catarrh, wouldn’t eat, had no energy and who were also positive reactors to the jelly test. To my surprise and delight they appeared to make very satisfactory progress and their mothers would come again and again for the “vitamin tablets”. As long as the treatment continued the catarrh was controlled, nocturnal nasal obstruction disappeared and there were no further infections of the throat or ears. If the tablets were discontinued the catarrhal state would soon relapse. In some cases treatment was used continuously or with intervals of abstinence for periods of a year or two with satisfactory results. As soon as I was convinced of the usefulness of rimifon, I decided to use it on all cases of catarrh and upper respiratory tract infections regardless of the result of the jelly test and it became evident that this test was not connected with the efficacy of rimifon. As I developed this therapy, I included para-aminosalicylic acid and its less unpleasant tasting derivatives

with even better results. In acute infections of bacterial type imposed on a background of catarrh, I used quarter strength therapeutic doses of antibiotics to act in synergism with rimifon. Meanwhile, certain investigations and much correspondence had found the jelly test to be inaccurate. I was rechecking my jelly positives with the same thought in mind and was finding them nearly all negative to Mantoux 1:1000. One year after the original tests with jelly I was to find a majority were again negative reactors to jelly. So my blundering researches had gone in a long, useless circle; but on the way I had picked up a very useful empirical treatment which has proved a boon to most patients, old and young, who suffer with catarrh and secondary infections from any mucous membrane of the body. The explanation of this successful empiricism was a puzzle. Could tuberculosis exist in a latent form which did not provoke a hypersensitivity reaction? Or could the bacillus of Koch have other life cycles than the classical one, which could be transmitted to the descendants of sufferers from tuberculosis. I knew that most of the families I looked after would not have to look further than parents or grandparents to find a death from tuberculosis. Supposing the tubercle bacillus could become granular or virus in form and, escaping through the meshes of the placenta, become resident in the foetal liver and spleen, causing only minor disorders such as neonatal jaundice, difficulty in thriving and delicacy in childhood? And supposing that these children growing up with a catarrhal diathesis produced by the presence of such a factor acting as a depressant to the defensive status, could continue to transmit a granular form across the placental barrier, yet with each generation this infection grew weaker and weaker as the opportunity for this form to metamorphose into the rod bacillus enclosed in its resistant lipoid capsule failed to appear, then the constitution would become stronger as the atypical and granular form of the tubercle bacillus grew weaker. If some such thesis were possible it would explain the response of the catarrhal state to anti-tuberculous drugs.

**Survey of Literature**

During the world pandemic of influenza in 1918, a number of research workers had attempted to prove that the influenza virus causing this epidemic was concealed by latency in the influenza bacillus and that by suitable culture techniques the latter could be persuaded to produce the virus in visible form again. These observations have fallen into neglect and even into disgrace because other workers using other techniques could not repeat them. The same workers who asserted that the influenza virus was a part of the life cycle of the bacillus of influenza were also able to demon-
strate an ultravirus which emerged from the bacillus of Koch when special culture techniques were applied\textsuperscript{3}. The opposition group, again using a different technique were unable to confirm these views. In 1933, M. C. Ninni was able to demonstrate non-acid fast atypical bacilli, both in micro-cultures and in vivo after inoculation of filtrates from tuberculous material and from cultures. He also found similar immature bacilli in the spleens and lymphatic systems of newborn guinea-pigs whose mothers were suffering from active and generalized tuberculosis. These atypical forms sometimes became acid-fast but did not cause tuberculosis nor did they cause a sustained hyper-sensitivity reaction to tuberculin. But they caused a disease which has variously been termed abortive tuberculosis, pre-bacillary, granulaemic or bacillose infection\textsuperscript{4}. More recently, in 1953, Negry and Bretey have again examined the facts regarding the transmission of a state of disease by some agent separated from tuberculous material by a filter or through a placenta and they have confirmed some of the earlier work. They deny that any virus is present, but they find evidence for immature bacilli passing these barriers. They confirm that tuberculosis does not develop but that a benign self-limiting disease occurs in guinea-pigs inoculated with the excreta and blood of infants born of tuberculous mothers and from the umbilical vein blood of the mothers filtered through Chamberland L 3 at more than 50 mm. mercury pressure. This state of disease does not progress and is not transmissible in guinea-pigs\textsuperscript{5}.

Downie and Meissner repeated some of Ninni’s work in 1934. They found that filtrates from various types of filter sometimes cause mild abortive pathologies in guinea-pigs and that passing material from these animals sometimes resulted in the development of tuberculous disease and positive cultures even when the original filtrates had apparently been negative microscopically and on culture. In other experiments a certain number of animals died of pneumonia not associated with tuberculous infection and an even larger number died of acute intercurrent disease, usually pneumonia, while being used as passage animals in serial inoculations of filtrates from other guinea-pigs. They concluded that defective filters will allow scanty numbers of immature bacilli to pass, but that efficient filters never do so\textsuperscript{6}. Ninni did not find a single filtrate to contain mature and pathogenic tubercle bacilli, nor did he observe congenital tuberculosis. Modern American opinion accepts the beading found in certain tubercle bacilli as being composed of living elements capable of developing into acid-fast bacilli in vitro and of causing tuberculosis in experimental animals\textsuperscript{7}. M. C. Kahn describes the development of tubercle bacilli together with non-acid-fast granules and rods in culture colonies. He has also described how the granules
can be observed in single-cell suspensions under a high power microscope to elongate to rods and to mature to acid-fast tubercle bacilli. On the other hand Cooper and Petroff failed to find any living agent in their filtrates from tuberculous material which would grow on culture medium or cause any disease in their inoculated animals. But Ninni, who was consistently successful in producing active pathogenic filtrates, insisted that crude saline filtrates would never be pathogenic. In effect, he anticipated the tissue culture medium now used to propagate viruses by rendering his filtrates active with the use of 5% saline and emulsified fresh liver and spleen pulp from healthy guinea-pig foetuses. No one repeated his techniques at that time and it is therefore not surprising that his successful results were not repeated. This was probably the reason for the failure of Downie and Meissner to confirm Ninni's work because they used only normal saline filtrates.

However, in 1949 Dr Brieger, working in the Papworth Hospital near Cambridge, reported some very interesting experiments using modern tissue culture techniques to develop tubercle mycobacteria from almost invisible granules found in caseous lesions from guinea-pig spleens. The animals had previously been inoculated intrasplenically with a large dose of virulent avian tubercle bacilli and allowed to recover. These animals were then sacrificed at intervals of many weeks subsequent to the inoculation. The lesions were examined histologically and bacteriologically. Very scanty or occasional mycobacteria were found after prolonged search; no culture was positive. Yet, within a few days of inoculating the material into tissue cultures, filamentous, mycelial, and finally typical acid-fast rod forms of the avian *M. tuberculosis* developed. In other words, *M. tuberculosis* disappears in one environment but can be persuaded to re-appear in another. This fully confirms the researches of M. C. Ninni.

Finally, in 1960, an American bacteriologist reported that mice which had been infected by human tubercle bacilli and had received treatment were free from viable tubercle bacilli when sacrificed at the end of a 90 day course of anti-tuberculous drugs. However, when kept for a further three months tubercle bacilli could be recovered by culture from sacrificed animals in the absence of any lesions or of obvious sources of bacillary infection.

To summarize this work; there is a case for suspecting that the bacillus of Koch is capable of more than one mode of reproduction according to the environment. In a *milieu* favourable to rapid growth the acid-fast bacillary rod segment and these by fission become granular and possibly ultra-microscopic. This amorphous, non-acid-fast material later becomes fine rods and only when the
environment is inimical do these rods acquire capsules and acid fastness. In tissues which are not hypersensitive, immature atypical forms would propagate. In order to transpose this experimental data to clinical form, it is suggested that the atypical rods or granular forms are passed by the mother with active tuberculosis through the placenta to the foetal liver and spleen. The females so infected may pass the same form to a new generation when they become parturient and so on. In each generation a certain number will develop primary endogenous tubercular foci if the granular form matures in the spleen and enters the general circulation to form emboli in the lungs. In the remainder, the presence of the granular form confined within the liver or spleen depresses hepatic function and is associated with a state of catarrh in the host. According to all experimental evidence the presence of the atypical bacillary or the granular form does not provoke a hypersensitive reaction to tuberculin and the Mantoux or Heaf test remains negative. It should be clearly stated that this hypothesis does not affect the classical mode of transmission of mature tubercle bacilli direct from host to host resulting in the primary, secondary, and tertiary phases of tuberculosis and accompanied by the conversion of tissue sensitivity to tuberculo-protein.

Published experimental work supports a hypothesis concerning the genesis of the catarrhal state by reference to a latent tubercle infection of atypical type. I suggest that empirical therapy with antituberculous drugs causes a reversal or suppression of catarrh. I do not intend to identify congenital hepatic and splenic infection by attenuated atypical viral particles or tubercle bacilli as the only cause of catarrh. Any agent, whether prenatal, neonatal, or in later life, which depresses hepatic function will initiate the catarrhal state. Alcohol causes cirrhosis of the liver accompanied by gastritis, oesophageal, pharyngeal, and bronchial catarrh. Tobacco smoking is sometimes associated with these catarrhal manifestations. Cessation of smoking results in an increase in appetite and marked weight gain; this could be due to improved hepatic function. The inhalation of impure air is known to be associated with the catarrhal state. It is possible that the agents inhaled are filtered off in the liver (the major organ of detoxification), thus causing slow but increasing loss of liver efficiency. The state of lassitude, anorexia, and depression ensuing after an illness (especially when of viral origin) may well indicate a depressed hepatic function not discernible by our crude biochemical tests.

Catarrh is an excess of mucoprotein normally excreted by endothelial membranes exposed to the environment of the body. Should the efficiency of the liver to de-aminise protein and to dispose of the products be reduced, it is possible that these membranes are used as
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an accessory organ of excretion. That this may be so is suggested by observing the reactions of new-born babies to their milk. Certain infants early manifest the catarrhal state. The first occurrence is the "sticky eye" of catarrhal conjunctivitis, localized to the inner canthus of one eye. Others commence with nasal obstruction, nasopharyngeal, or pharyngo-oesophageal catarrh. A little later these babies regurgitate feeds, retch mucous fluid, or frankly vomit. Analysis of their feeding habits will disclose that the calorie intake is excessive, or that, although the calorie/weight ratio is correct, they are much overweight. A short fast followed by adjustment of the feeds causes a regression of the catarrhal state. No drug therapy is necessary. I suggest that the catarrhal state is an expression of poor hepatic function associated with protein metabolism. It follows that any biological or chemical agent which depresses liver function with reference to protein economy and disposal may produce the catarrhal state. Atypical tuberculosis can be inherited or acquired; it is chiefly thought to infect the liver, spleen, and lymphadenomatous systems and by this means to depress the liver function and cause catarrh.

The Clinical Picture

In general it is a condition of subnormal health very commonly seen in general practice which develops when the level of health fails to be maintained. The body defences are re-aligned on a new basis to resist further deterioration resulting in a state of catarrh developing at various weakened areas situated on the main canals of the body—the gut, the respiratory, or the genito-urinary systems. Descent into the catarrhal state commences in the autumn and emergence occurs in the spring. Catarrh is like syphilis in that it can affect all ages and many systems; syphilis is a spirochaetemia with hepatic and splenic infection which accords well with the hypothesis expressed in this paper concerning atypical granular hepatic infection by the bacillus of Koch. The symptoms of catarrh are numerous, but the signs are scanty. The clinical symptoms define a state of poor physiological function accompanied by mucoprotein hypersecretion in endothelial membranes which are liable to acute exacerbation through bacterial infection.

The Respiratory Tract

The primary catarrhal syndrome is a cold antiphlogistic affair, there being no fever and no tumescence. But ear, nose, and throat areas are very liable to develop secondary inflammatory reactions. Bronchial catarrh and bronchitis, atelectasis and pneumonitis, sinus catarrh and sinusitis are examples of this dual cold and hot pathology. Obstructive nasal catarrh extending to the eustachian tubes causes tinnitus, impaired audition and pains beneath the ear canals. A
catarrhal otitis media occurs with a grey sodden ruptured membrane and a mucoid discharge without fever and with little pain; an exudative eczema of the ear canal sometimes occurs. Catarrhal sinusitis produces a radiological shadow of lesser intensity than does empyema; the middle turbinate is collapsed, pale, and covered by a grey pellicle. Tonsil and adenoid tissue in the nasopharynx is hypertrophied and glands in the anterior cervical triangle are enlarged in children between 4 and 7 years, although it is a rule that these signs of the catarrhal state subside after this age. When the oesophagus or trachea are affected there is a dry, whistling cough in explosive and repeated spasms which occur readily after meals or soon after retiring at night. The spasms often interrupt breathing, causing eye watering or retching. Changes of atmosphere are liable to precipitate an attack and in children it can cause whooping spasms which imitate pertussis. Bronchial catarrh is too well known to require description. When catarrh affects the lung parenchyma a state of atelectasis develops, if inflammatory bacterial reaction sets in, then bronchitis, bronchopneumonia, or pneumonitis is imposed upon the catarrh.

The gastro-intestinal tract syndrome

The first symptom can commence as early as one month of age and is often precipitated by overfeeding during the first 6 months and is manifested by nasal obstructive catarrh which interferes with feeding. When the pharynx is affected there is gagging, hawking, and a tendency to develop short spasms of choking cough while taking feeds or in older patients during mealtimes. Oesophageal catarrh causes a dry, tickling, hollow cough after meals or shortly after lying down to sleep. Older patients complain of pain in the region of the mediastinum or at the xiphisternal notch. A lump is sometimes felt at the level of the interclavicular notch and the patient is constrained to hawk up or swallow down tenacious mucous from this level. Breathing fast or hurrying or the act of coughing sometimes provokes a retching attack which raises fluid and mucous and sometimes provokes the stomach to evacuate a meal by vomiting. When the catarrhal state reaches the stomach there are complaints of fluttering, or weakness in the upper abdomen, of a bloated sensation, of normal or increased appetite which is too readily satiated and followed by distension after even a very meagre meal. Flatulence and epigastric discomfort are usually not related to meal times. If vomiting does occur the vomitus consists more often of slimy, watery fluid rather than of food. When duodenitis is present the symptoms of nagging pain in the epigastrium between meals which is relieved by alkalies and frequent feeds are confirmed by negative radiological findings. Regional ileitis with its non-
specific pathology, congestive inflammation of the mucosa, and multiple, local adenitis is another possible expression of the catarrhal state. Many sufferers from chronic constipation and spastic colon pain become frank cases of mucous colitis, which is surely another form of the same catarrh. All these states can develop at any age from birth onwards, appearing and regressing from season to season and in accordance with the general health of the patient. They tend to prevail at the change of the seasons when such are described as "chills", or following circumstances which cause nervous or physical depression of the patient's vitality. The syndrome may be observed to travel from the mouth to the anus as interrupted episodes taking years to extend to other areas and often recurring repeatedly at one site before affecting a new region. It seems likely that the vague symptoms of pain in the right iliac fossa, constipation, and dyspepsia which has been called "grumbling appendicitis" are caused by catarrh and muscle spasm of the caecum and appendix. Should a hot inflammatory defence reaction be initiated by bacterial infection then acute appendicitis occurs and the local catarrhal state is liquidated.

The reproductive system

Catarrh of the vulva and vagina is not uncommon in young children and is reported by the mothers who are worried by finding stains on undergarments. Leucorrhoea of catarrhal type commences after the menarche, but in multiparous females is accompanied by secondary bacterial infection following trauma to the cervix during a birth. The endometrial proliferation which is often found to accompany cervicitis may indicate a catarrhal metritis. The symptoms associated with such a pathology are polymenorrhoea, menorrhagia, dysmenorrhoea, and chronic sacral discomfort. Sometimes painless bladder frequency, precipitant micturition, or cough incontinence indicate a state of trigone catarrh, while frank attacks of cystitis are caused by the usual secondary infection invading a mucous membrane already weakened by catarrh. Such patients often exhibit multiple symptoms suggesting a general lowering of vitality usually called nervous debility. There is epigastric emptiness and unusually rapid satiation at meals so that although feeling hungry a few mouthfuls satisfies them. They complain of central abdominal bloating causing them to cast off corsets. They are moody, irritable, perpetually tired, yet unable to sleep soundly. They are prone to miscarriage and accidental haemorrhage in pregnancy; many are relatively sterile.

General aids to diagnosis

Wherever the catarrhal state is manifest, there one finds local lymph gland hypertrophy and tenderness. The cervical, the mesenteric and the internal chain of iliac glands are all palpable if the
catchment organs are affected by catarrh. There is also a tendency for inflammation due to known pathogenic bacteria to develop at any site sick with catarrh where such organisms are saphrophytic or can gain access. Such a duel pathology is illustrated by tonsillitis, sinusitis, and otitis media in the upper respiratory tract; by bronchitis, bronchopneumonia, and pneumonitis in the lower respiratory tract; by infantile gastro-enteritis and by some cases of ulcerative colitis; by vaginitis, cervicitis, and cystitis in the genito-urinary tract. It is suggested that some states of catarrh and secondary bacterial infection result from excessive secretion of mucoprotein initiated by a general decrease in hepatic function.

In general, these patients are tense and irritable. They tire easily but sleep lightly. They cannot face any meal before midday and although feeling hungry a small meal satisfies them. Headaches are a common occurrence. Among parous women enquiry will elicit menstrual irregularities. Adolescent and young adult males are immune except for the digestive tract.

Perhaps the experimental work described in this paper has been ignored or misunderstood because the phenomena observed in experimental animals did not appear to relate to any diseases or syndromes described in man. Pioneers report facts for posterity to interpret. If the successors and students of Koch have reported some part of the truth when they observed that the foetuses and young of guinea-pigs infected by human tubercle bacilli were not healthy because of liver damage, then we must look for a similar syndrome in humans. The syndrome we are looking for may be the catarrhal state and this state may be an occult defect in protein metabolism.

REFERENCES