Mining the History of Medicine

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Outline

- Text Mining tools for enriching content
- Mining the History of Medicine
- Semantic annotations:
 - entities, events
 - OCR correction
 - Time-sensitive term inventory and search
- A prototype search system for the history of medicine

Mining the History of Medicine

- National Centre for Text Mining, School of Computer Science <u>www.nactem.ac.uk</u>
- Centre for the History of Science, Technology and Medicine



Semantic search system

- British Medical Journal (BMJ) (1840 present) (350K articles)
- London Medical Officer of Health reports (MoH) (1848 – 1972)

Text Mining: tools, resources, infrastructure

Provide **different perspectives** (e.g. medical, public health) on the treatment and prevention of diseases

- \checkmark over time
- \checkmark in different areas

Aim



Solutions

- ✓ Apply OCR improvement techniques
- Automatically detect semantic information in text
 - ✓ Entities: conditions, signs or symptoms, therapeutic measures
 - ✓ *Events:* symptoms caused by lung disease
- Automatically identify how the naming of concepts changes over time

Semantic search system ✓ Automatic query building, term suggestions

- historical variants unknown to the user
- ✓ Faceted search based on article metadata
 - Date, authors, title
- ✓ Faceted search based on semantic content
 - Combinations of entities and/or relationships

OCR Post Correction

- Re-OCR BMJ too time consuming for current project
- Our solution: post-correct original OCR output based on spell-checker output

SpellChecker	% errors resolved	Best open source spell checker
ASpell	45%	
Hunspell	60%	
Word	63%	
MAC OS	58%	



Override default Hunspell correction ranking

- ✓ Rank suggestions according to **corpus frequency**
- ✓ Use **decade-specific word frequency** lists

BMJ OCR Errors – Example from 1840

JOHN MILLER, aged 26, glass-blower of Gateshead, was adnmitted August 27th, 1840, unider the care of Sir John Fife, with the usual syptness of stone in the bladder, wlich he lhas laboured under from childhood. At the age of 12 years he was admitted into thtis infirmaryI, buit his frienids wotld niot allow the operation to be performed. Ile took a considerable (luantity of medicine, which greatly relieved him. Since then the symptomt of stone have been constantly present, but have not been very urgent. A.- About a month ago, after batlhing, the symptoms became much arggravated-so much so, as to comlpel him to apply again to the hospital for relief. On admission he was sallow and emaciated; laboured iunder symptoms of stone of a high degree, with great irritability of bladder, giving rise to a frequient desire to inicturate, and occasionally to the in-voluntary discharge of faces from straining. Ile passed a larg, e quantity of mucus with his urine; -pulse small, tongue white, slight thirst, and appetite good.

Basic Hunspell Output

Correct changes

made by Hunspell JOHN MILLER, aged 26, glass-blower of Gateshead, was admitted August 27th, 1840, under the care of Sir John Fife, with the usual **symptoms** of stone in the bladder, which he has laboured under from childhood. Af Incorrect changes 12 years he was admitted into this infirmary, made by Hunspell friends world into allow the operation to be performed. **Ike** took a considerable (quantity of medicin, which greatly relieved him. Since then the **symptom** of stone have been constantly present, but have not been very urgent. A.- About a month ago, after **bathing**, the symptoms became much aggravated-so much so, as to compel him to apply again to the hospital for relief. On admission he was OCR Errors not sallow and emaciated; laboured under svr of detected by a high degree, with great irritability (ing rise to a frequent desire to **inaccurate**. Hunspell llv to the involuntary discharge of faces from straining. Ike passed a lag, e quantity of mucus with his urine; -pulse small, tongue white, **slight thirst**, and appetite good.

New Frequency-driven Hunspell Output

Corrections only Corrections lass-blower of Gate JOHN MTL obtained using obtained using admitted .840, under the care both original and frequency-driven Fife, wi mptoms of stone in method frequency-driven which he has aboured under from childh a 12 years he as admitted into this infirmary, but his friends would not allow the operation to be performed. Lie took a considerable (quantity of medicine, which greatly relieved him. Since then the **symptoms** of stone have been constantly present, but have not been very urgent Remaining About a month ago, after bathing, the symptoms errors with aggravated-so much so, as to compel him to appl frequency-driven the hospital for relief. On admission he was sa methods emaciated; laboured under symptoms of stone of degree, with great irritability of bladder, giving rise to a frequent desire to inaccurate, and occasionally to the involuntary discharge of faces from straining. Lie passed a large, e quantity of mucus with his urine; -pulse small, tongue white, slight thirst, and appetite good.

Avoiding Over-Correction

Original Text	Basic Hunspell	Frequency- driven Hunspell	Frequency-driven Hunspell augmented with OpenMedSpel
antithrombotic	anthropometric	anthropometric	antithrombotic
pathophysiological	physiological	physiological	pathophysiological
thromboembelism	thrombosis	thrombosis	thromboembolism
warfarin	wayfaring	warfarin	warfarin
transoesophageal	oesophageal	oesophageal	transoesphageal
echocardiography	electroocardiography	oesophageal	echocardiography
intracardiac	intra cardiac	intracellular	intracardiac
tomogram	mammogram	tomogram	tomogram 13

Evaluation

 ✓ Gold-standard collection of 24 handcorrected documents
 ✓ 3 documents from: 1840s, 1860s, 1880s, 1900s, 1920s, 1940s, 1960s, 1980s
 ✓ Documents selected according to likelihood containing OCR errors

Evaluation (Word Level Accuracy)

PMCID	Raw OCR	Basic Hunspell	Frequency- driven Hunspell	Basic Hunspell with OpenMedSpel	Frequency- driven Hunspell + OpenMedSpel
1840s	75.9%	83.6%	84.9%	83.3%	85.6%
1860s	86.6%	90.0%	91.2%	90.2	93.1%
1880s	82.6%	87.4%	88.9%	88.0%	89.0%
1900s	70.2%	80.7%	82.3%	81.7%	84.3%
1920s	74.2%	79.9%	82.7%	81.6%	84.3%
1940s	86.6%	88.1%	89.5%	89.4%	91.3%
1960s	94.9%	91.9%	93.5%	95.1%	95.7%
1980s	93.0%	87.2%	89.9%	92.6%	94.8%

Rule-based OCR correction

- ✓ Many regular OCR character recognition errors occur in BMJ
 - Two characters being recognised instead of one,
 - e.g. *h-> lh, t-> lt, m->mn, u-> ui*
 - Punctuation characters/digits erroneously appearing in words
 - e.g. *larg,e*
- Many character insertion problems corrected by Hunspell
 Still some regular errors remain uncorrected
- Solution apply rule-based pre-processing prior to Hunspell

Rule-based OCR correction

- ✓ Eight pattern replacement rules, i.e., $tll \rightarrow th$, $wl \rightarrow w$, $lh \rightarrow h, hl \rightarrow h, mn \rightarrow m, nm \rightarrow m, wv \rightarrow w$ and $ii \rightarrow l$
- Remove punctuation characters and digits appearing in words, except when:
 - Digits are followed by letters denoting ordinal numbers not removed
 - Apostrophes denoting possessives not removed
 - Hyphens are only removed when they occur as the second or penultimate character of a word.
 - Hyphens in other positions are likely to form part of valid hyphenated words

Evaluation (Word Level Accuracy)

PMCID	Frequency-driven Hunspell + OpenMedSpel	Frequency-driven Hunspell + OpenMedSpel + Rule-based pre-processing			
1840s	85.6%	87.0%			
1860s	93.1%	94.1%			
1880s	89.0%	90.5%			
1900s	84.3%	86.2%			
1920s	84.3%	87.6%			
1940s	91.3%	92.3%			
1960s	95.7%	94.2%			
1980s	94.8%	92.7%			
Customised OCR Correction for Historical Medical Text Digital Heritage 2015					

Extracting semantic types, events



✓ Corpus composition

- 25 articles from BMJ
- 4 extracts from MOH
- 70,000 words
- ✓ Articles from 4 key decades
 - 1850s, 1890s, 1920 and 1960s
 - Capture language/terminology changes over time

HIMERA corpus: Entity Types

Туре	Description	Examples
Anatomical	An entity forming part of the human body	lung, lobe, sputum, fibroid
Biological_ Entity	A living entity not part of the human body	tubercle bacilli, mould, guinea-pig, flea
Condition	Medical condition or ailment	phthisis, bronchitis, typhoid
Environmental	Environmental factor relevant to incidence/prevention/ control/treatment of condition	humidity, high mountain climates, milk, linen, drains
Sign_or_ Symptom	Altered physical appearance or behaviour as a probable result of injury or condition	cough, pain, rise in temperature, swollen
Subject	individual or group of cases under discussion	asthma patients, those with negative reactions to tuberculin
Therapeutic_ or_ Investigational	treatment, substance, medium or procedure, prescribed or used in investigation	atrophine sulphate, generous diet, change of air, lobectomy 20

HIMERA Corpus: Events





Entity Agreement Rates (F-Score)

Туре	Exact span agreement	Relaxed span agreement
Anatomical	0.81	0.85
Biological_Entity	0.99	0.99
Condition	0.92	0.95
Environmental	0.63	0.79
Sign_or_Symptom	0.84	0.88
Subject	0.70	0.81
Therapeutic_or_Investigational	0.73	0.78
TOTAL	0.80	0.86

HYMERA annotation counts

Entity Type	Count
Anatomical	2002
Biological_Entity	295
Condition	1499
Environmental	1268
Sign_or_Symptom	1171
Subject	1062
Therapeutic_or_Investigational	1046
TOTAL	8343

Event Type	Count
Affect	611
Causality	204
TOTAL	815

- Discrepancies in double annotated docs resolved
- Anatomical entities most numerous
- Biological_Entity sparse according to rare mention of microorganisms prior to 20th century

Entity recognition – NERSuite

- ✓ Entity Models trained NERSuite nersuite.nlplab.org
 - Pre-processing using GENIA tagger to generate features
- ✓ Default features for learning
 - Surface word forms
 - Base word forms
 - POS tags
 - Syntactic chunk tags
- ✓ Default features augmented with semantic features

Entity recognition Models

- ✓ Baseline (BL) Default NERSuite features
- ✓ Full MetaMap (FM) Semantic features added by applying MetaMap semantic tagger (133 types)
- Selective MetaMap (SM) Semantic features added by mapping selected MetaMap categories to the seven HYMERA entity categories
- UMLS Lookup (UL) Semantic features assigned using dictionary lookup in filtered version of the UMLS Metathesaurus dictionary.

UMLS -> Corpus Mappings

MetaMap Categories	Hymera category
Anatomical Abnormality, Body Substance Body Part, Organ, or Organ Component Body Location or Region, Body Space or Junction, Tissue	Anatomical
Animal, Mammal, Cell, Bacterium, Organism	Biological_ Entity
Food, Chemical Viewed Structurally Element, Ion, or Isotope, Hazardous or Poisonous Substance Substance, Natural Phenomenon or Process	Environmental
Disease or Syndrome, Pathologic Function	Condition
Clinical Drug, Amino Acid, Peptide, or Protein, Immunologic Factor, Organic Chemical, Pharmacologic Substance, Biologically Active Substance, Lipid	Therapeutic_or_ Investigational
Sign or Symptom, Finding	Sign_or_ Symptom
Group, Patient or Disabled Group	Subject

NERSuite Results (F-Score, 5-fold cross validation)

Туре	BL (Exact)	BL (Relaxed)	UL (Exact)	UL (Relaxed)
Anatomical	0.73	0.79	0.76	0.83
Biological_Entity	0.70	0.72	0.74	0.75
Condition	0.73	0.82	0.77	0.86
Environmental	0.49	0.58	0.49	0.60
Sign_or_Symptom	0.66	0.71	0.69	0.74
Subject	0.74	0.81	0.75	0.81
Therapeutic_or_Investigational	0.57	0.64	0.61	0.67
ALL	0.67	0.74	0.70	0.77

UL results reported as most straightforward model to apply MetaMap can be slow

Comparison

✓ Anatomical F-Score 0.82

- ✓ Comparable with anatomical entity recognition for (0.85 F-Score) (Pyysalo & Ananiadou, 2014)
- ✓ Condition F-Score of 0.76 (exact) and 0.86 relaxed
 - ✓ Comparable to disease recognition performance for electronic health records (0.75 exact/0.88 relaxed) (Kaephwan et al., 2014)

Pyysalo S, Ananiadou S (2014) Anatomical Entity Mention Recognition at Literature Scale. Bioinformatics 306:868–875

Kaewphan, S, Hakala, Kai and Ginter, F (2014) UTU: Disease Mention Recognition and Normalization with CRFs and Vector Space Representations, In Proceedings of the 8th International Workshop on Semantic Evaluation (SemEval 2014), pp. 807—811

Time-sensitive NER experiments

- ✓ How time-sensitive is NER?
- ✓ Split the HIMERA to decades
 - ✓ Used docs from a single decades as test data
 - Trained on combinations of docs from other decades

Time-sensitive NER example (Testing on 1890s docs)

	Training Data					
Туре	1850s	1920s	1960s	1850s /1920s	1920s /1960s	1850s /1920s/ 1960s
Anatomical	0.78	0.66	0.53	0.83	0.66	0.84
Biological_ Entity	0.41	0.87	0.13	0.88	0.92	0.91
Condition	0.79	0.77	0.72	0.85	0.67	0.85
Environmental	0.32	0.26	0.23	0.38	0.29	0.44
Sign_ or_Symptom	0.68	0.56	0.41	0.72	0.54	0.72
Subject	0.79	0.73	0.68	0.80	0.72	0.78
Therapeutic_or_ Investigational	0.35	0.39	0.19	0.47	0.33	0.52
ALL	0.70	0.64	0.51	0.76	0.61	0.77 ³¹

Observations

- $\checkmark\,$ Similar pattern when different decades are test set
- $\checkmark\,$ When single decade used for training
 - Best results normally when decade immediately prior to test data is used for training
- $\checkmark\,$ When two decades used for training
 - Best results usually when decades surrounding test decade are used for training
- ✓ Best overall results when 3 decades used for training
 - But, usually only small performance difference from two surrounding decades
- <u>Temporal closeness</u> of training and test data more important than volume of training data
- As long as some temporally close training data is included, it is not harmful to include training data from more distant decades

Event Recognition

- EventMine www.nactem.ac.uk/EventMine/
- Detects triggers: origin
- Finds individual event participants
- Combines trigger-argument pairs into semantic structures



Event trigger recognition performance

Event Type	F-Score (Exact)	F-Score (Relaxed)
Affect	0.40	0.45
Causality	0.19	0.27
TOTAL	0.35	0.42

- Much sparser data than previous EventMine applications
- Event types have wide semantic scope
- Diverse range of triggers and stylistic variations can make recognition a challenge
- Events with multiple participants recognised

Ongoing annotation efforts

Ongoing work to triple the size of manually annotated corpus

- Different decades to provide greater evidence of language usage
- More events

History of Medicine Terms

✓ Concepts can be expressed in many ways

✓ We take into account such variants to improve search

Lexical Variations	
oedema	edema
whooping cough	whooping-cough
pulmonary tuberculosis	tuberculosis
respiratory diseases	diseases of the respiratory system
Semantic Variations	
tuberculosis	phthisis
smallpox	variola
Building a Time Sensitive Terminological Resource

- ✓ Why not using existing resources?
 - MeSH, Disease Ontology, UMLS, Metathesaurus
- ✓ Used in search systems to *expand query terms*
- ✓ Textual variants of concepts change over time
 - Existing resources tend to focus on contemporary terminology
 - **Historically-relevant** variants not covered in a comprehensive and consistent manner

Term Variation in BMJ *Phthisis* vs. *Tuberculosis*



Term Variation in BMJ Scarlet Fever vs. Scarlatina



Time Sensitive Terminological Inventory

✓ Time sensitive inventory of medical terminology

- Complements existing terminological resources
- Accounts for term variants over time

✓ How?

- Extracted term variants from 19th c. medical lexica
- Identified more variants using *distributional semantics* to BMJ and MOH archives

Processing Historical Lexica

19th century medical lexica: NLM Archive

Name	Year	# top-level entries	
Nomenclature of diseases	1872	1347	
Index of diseases, their symptoms, and treatment	1882	522	

Processing Historical Lexica - example



Processing Historical Lexica

✓ Link UMLS concepts to historical concepts

• approximate string matching

✓ 1,588 UMLS and historical concepts linked

- 2,422 historical synonyms/variants not in UMLS
 - e.g., cerebro-spinal fever as a synonym of epidemic meningitis <u>only</u> in historical resource
- ✓ 800 historical concepts could not be linked to UMLS concepts
- ✓ lack of comprehensive historical coverage in UMLS

Need for Distributional Semantics

- ✓ Different lexica to account for terminology usage in different time periods
- ✓ Distributional semantics techniques –
- ✓ Processed complete BMJ and MOH archives to extract semantically related terminology across complete archive time-span

TM Methods for Historical Variant Identification

✓ Pre-processing

✓ Distributional similarity measures

Detection of historically relevant term variants

Pre-Processing

- ✓ Extracted disease terms
- ✓ Combined 2 disease NERs
- ✓ Dictionary matching from 19th lexica
 - ✓ Index of Diseases
 - ✓ Nomenclature of Diseases
- ✓ Trained on NCBI Disease
 Corpus



Distributional Similarity Measures

✓ Generate Context vector for each term

✓ 6 word window around term

✓ High cosine similarity between context vectors indicates related terms

scarlet fever	47366.48	46344.15	30555.26	31896.95	15241.49	11759.56	7407.69	7388.65	 4608.19
	measles	diptheria	fever	cough	death	рох	fatal	small	 typhoid
	11474.87	5436.11	5434.60	2892.64	2413.52	4326.59	875.16	2340.05	 2071.56
scarlatina	measles	diptheria	fever	cough	death	рох	fatal	small	 typhoid
		cos	(heta) =	$=\frac{A}{\ A\ }$	$\cdot B$ $ B $	= 0.	8434		

Distributional Similarity Measures

scarlet fever

scarlatina 0.8434 whooping cough 0.7415 measles 0.7094 diphtheria 0.6689 acute pneumonia 0.6501 chicken pox 0.6407 german measles 0.6336 diarrhoeal disease 0.6301 infantile diarrhoea 0.6234 diarrhea 0.6208 croup 0.6093 mump 0.6042 typhus fever 0.5535

...

Automatic Evaluation of DSM output

✓ Use UMLS Metathesaurus

- ✓ At least one UMLS synonym is identified >70% cases
- ✓ MOH reports, all synonyms listed in UMLS discovered by the DSM method in 49% of cases

Expert Evaluation of DSM output

- Automatic evaluation general performance of DSMs
- ✓ However
 - No historical synonym coverage
 - No other types of semantic relations between related terms
- ✓ Expert evaluation covers
 - 348 source-target term pairs examined by expert, with cosine similarity greater than 0.8
 - Only 18% identified as synonyms using UMLS
 - Expert asked to characterise semantic relation (if any) between the two terms

Possible relations between terms



Unrelated

Expert evaluation results

Event Type	Count
Synonym	83 (24%)
isA	21 (6%)
isParent	35 (10%)
Affects	10 (3%)
isAffectedBy	11(3%)
Spatially Related	19 (5%)
OtherRelation	35 (10%)
TOTAL SEMANTICALLY RELATED	216 (62%)
Unrelated	106 (30%)
Non-disease pair	26 (7%)

- Expert identified more synonyms than UMLS
 - DSM can identify more synonyms
- ✓ 62% of pairs semantically related

Semantic annotation of archives

- Integrated: OCR correction, NER, event into interoperable pipeline for medical history
- Automatically recognised NEs used as input terms to DSM methods
 - Recognised semantic relations between a large number of medical terms belonging to different semantic classes
 - Created a wide coverage, historically-aware resource of medical terminology

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Search My Documents

Search Query

Term
pulmonary consumption

x

User (partially) completes template according to the types of events they are searching for. Here, the search is for documents mentioning causes of tuberculosis

Related Terms

non ni

primary pulmonary tuberculosis

Please enter causality event argu	iments	
CAUSE		
causes		
tuberculosis		
in		
SUBJ		

Document display





Pie chart shows the distribution of entity types in a document. Hovering the mouse over a section reveals the entity type in question

Co	nten	t

Content		Entities
THE attention.		
370 Medical JOURNAL I		 Anatomical (37) Biological (32)
INTERNATIONAL MEDICAL CONGRESS:		animal (1)
.*~~~~.		bacilli (4) bacillus (7)
[AUG. 16, I913.'		bovine bacillus (2)
	Number of	cow (8) guinea-pig (2)
THE NECESSITY FOR A MORE THOROUGH	"Environmental" entities	human bacillus (4)
CONTROL OF THE MILK SUPPLY IN COMBATING SURGICAL TUBERCULOSIS	in the document	organism (1)
IN CI	in the document	tubercle bacilli (3) Condition (71)
^{вун} "Environmental" entities		Environmental (22)
sur are highlighted CHILDREN.		cow (1) dust (1)
0 0	ne valuable work in developing the methods by means of wilicih	gold daledalin (1)
we a sis is of Halliman or b		infective material (1) milk (13)
Professor Delepine has for several years carried out ii-antiport investigations in Mano		milk product (1)
shown that mucll still remains to be done to diminish0 the amount of tuberculous mil	k which is supplied to our large cities.	raw milk (1) rural district (2)
The control of tile Edinburgh milk supply is very inadequate, and it is a remarkable fa Public Health Department has no power to enforce the laughter of tile cows with tur-	ct that the.	tuberculous milk (1)
from time to time in the city byres; the medical officer of health has merely power to boundaries.		Sign of Cympton (2)
	"Environmental" entity	case (29)
Fortunately comparatively large quantities of the bacilli are necessary to produce tu even -more prevalent amongst children tllan it is.	instances in the document	child (21) consumptive patient (1)
Post-or0tem records in this country show tilat in about 25 per cent. of the children possessing tuberculous lesions the infection has taken place through	the almontary tract.	given case (1)
As the result of my clinical experience in the Royal Edinburgh Hospital for Sick Child		young child (1)
disciples committee a serious error in practically disregarding the milk as a source of	f tuberculous infection in children.	Therapeutic or Investigational (19)
I could adduce many instances from my own personal observation where the etiolog	lical relations between the disease and the "milk history " of the	

I ne earliest observation on the contagious nature of tuberculosis occurs in the Ordinances of Ivian in India, thirteen centuries B.O. In these, pulmonary consumption and swelling of the glands of the neck are declared to be unclean, incurable diseases.

Those who wanted to marry are cautioned not to select a spouse from a consumptive fancily even though the family had a good lineage and possessed great wealth.

These laws show a knowledge of tuberculosis, and as the disease was regarded as an impediment to marriage it seems likely that it was regarded as contagious.

In Europe the earliest reference to the contagious nature of tuberculosis was made about 390 B.C.

In this he states: "The majority of those who had nursed this disease [phthisis] had did not generally subscribe to this view, preferring the idea of the tuberculous diath About one hundred years later Aristotle realized that consumption could be spread Galen and Avicenna held similar views.

Cases where specific causes of tuberculosis are mentioned in the document

It is more than a tragedy that these early Greek observations were disregarded and forgotten in later centuries, for it was only towards the end of the seventeenth century that in Latin countries such as Spain and Italy the contagious nature of the disease was again being recognized.

In Britain, Edward Mainwaring was possibly the first to assert that tuberculosis was spread by contact, as in 1667 he wrote: "You must not frequently converse with a phthisical person whose unwholesome breath may infect the sound by drawing in put-id vapours which the other breathes forth, but above all a phthisical bedfellow is most dangerous to affect a sound person and chiefly to be avoided."

Later, in 1694, Richard Morton in his book Phthisis logia, which is an outstanding presentation of the symp symptomatology of tuberculosis, wrote: " A contagious principle also propagates the disease, for, as I have found by experience, an affected person may poison a bedfellow by a kind of

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cond

Phrases identifying Causality events are highlighted

ineteenth century, however, leaders of the profession like Bright and Addison (1839), sness of tuberculosis, and attached great importance to diathesis. dominated men's minds that little or no progress had been made for centuries

rsity of London on March 6, 1947.

urred the disease was tuberculosis, was of the opinion that at least in France

tuberculosis was not usually con contagious.

That tuberculosis could be produced in animals by inoculation with tuberculous material was shown in 1843 by Klenke, and in 1868 Villein finally proved experimentally that tuberculosis was an infectious disease.

It was Villein who first showed that tuberculous material from bovine sources was more virulent for rabbits than' that from human. In 1867 William Budd, of North Tawton, as a result of a study of the geographical distribution tion of consumption in past and present times, concluded: "The tuberculous matter itself is (or includes) the specific matter of the disease and constitutes the material by which phthisis is propagated from one person to another and disseminated throughout society." Even after the dis cover of the tubercle bacillus by Koch- in 1882 we find from the Collective Investigation Record (British Medical Association, 1883) that many British physicians reported that they had never observed a case of probable trans mission of the disease' from a case of phthisis.

Later, Theobald Smith (1896, 1898) reported the existence of " a distinctively human or sputum, and a bovine variety of tubercle bacillus."

Though Koch proved that the tubercle bacillus was the cause pecans and stressed the importance of inhalation of infected sputum in the spread of the disease, it is strange how in 1901, while accepting that- human and bovine types were different, he yet concluded that the latter was rarely pathogenic for man.

Koch (1882) had undoubtedly found the bovine bacillus in human disease, for he had obtained from a case of caseous pneumonia (No.

27) a culture of tubercle bacilli which after inoculation into the anterior chamber of the eye proved virulent for rabbits.

In 1911 the British Royal Commission proved conclusively that the bovine bacillus was a definite cause of tuberculosis in man.

It is not surprising that Koch went astray when we consider the relative rarity of primary abdominal tuberculosis in Germany as compared with this

Causality (11)

Course

- inoculation causes tuberculosis
- bovine bacillus causes tuberculosis
- inhalation causes respiratory tuberculosis

of loo!

- Cause of meningitis
- Caused by infection
- Caused by treatment
- Caused by infection
- Cause of respiratory tuberculosis
- Cause of infection
- Cause of tuberculosis

Prophylactic vaccination with B.C.G. is still a controversial question, and over 20 years of trial has left the medical profession in a state of confusion as regards its efficacy.

Many reports, chiefly from Scandinavia and more recently from America (Aronson and Palmer, 1946),.

and the recent Memorandum to the Minister of Health (Tytler, 1946) testify to the advisability and the adequacy of this n It is uncertain, however, that in a mixed population such as ours the same results would hold as elsewhere, particularly prevalent disease with us, and frequent infection must be the lot of us all.

The discovery by Petroff et at.

(1927-8) that B.C.G. could dissociate into avirulent R and virulent S forms raised.

doubts in the minds of many regarding the use of a living vaccine.

No definite case of tuberculosis has, however, yet been proved as resulting from the use of properly prepared B.C.G. va Vaccines of killed bacilli have been employed with apparent success by Goodwin and Schwentker (1934), Opie et al. (19 As in all tuberculosis research, it will be long before we can assess and pass a final judgment on the efficacy of B.C.G. This interval must be at least 15 to 25 years in order to allow us to judge its efficacy in the young adult age group, in wh such a serious problem.

Meanwhile, B.C.G. may serve a useful function until chemotherapeutic or immunological research provides us with som of tuberculosis as penicillin has been for pyogenic infections.

In his Memorandum Tytler (1946) has given all the essentials for a scheme of prophylactic vaccination.

It is hoped that those in authority will carefully consider his suggestions, as the disaster at Liebeck is still fresh in our mi

With regard to the cure of established tuberculous disease, nothing can be added to the valuable contribution which D'.

the chemotherapy

of tuberculosis. Streptomycin is still under trial Affect events allow us to explore, e.g., whether therapeutic measures have a positive or negative effect

aited with interest.

Events

- Affect (7)
- Effect on cell
- Affected by malnutrition
- Effect on fibrosis
- Affected by tuberculin
- Affected by infection
- Affected in child
- Affected by vaccine
- Causality (11)

Conclusions

✓ Explore further archives using topic analysis

- ✓ Automatic clustering of search results according to similarities of semantic content
- ✓ Expand types of entities and events and enrich further BMJ
- ✓ Link with other archives
- ✓ Create a rich annotation database

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